

# COVID-19 Critical Triad:

## Gut Microbiome Disruption, Vitamin D Deficiency, Altered RAS/ACE2 Axis

### SYSTEMIC EFFECTS (Especially on elderly and patients with co-morbidities)

- Dysfunctional Gut-Lung axis
- Increased predisposition to infections and malignancy
- Decreased antiviral and antibacterial activity
- Increased risk for gut dysbiosis, autoimmune, inflammatory disorders
- Increased severity in COVID-19 sepsis
- Poor response to vaccinations

### GUT DYSBIOSIS

- Lack of balance between pro and anti-inflammatory activity
- Altered intestinal membrane integrity and barrier function
- Impaired immune cell production and function
- Increased inflammatory cytokines and dysfunctional gut-lung axis

### VITAMIN D DEFICIENCY

- Dysregulation of RAS/ACE2 axis, causing hyper-inflammatory state
- Disrupts microbiome and protective gut barrier activity (with decreased ACE2 signaling pathway)
- Lack of differentiation and function of immune cells
- Together with disruption of gut microbiome further exacerbates immune system and cytokine storm

### ALTERED RAS/ACE2 AXIS

- Increased Renin/RAS/ACE activity
- Increased Angiotensin I and II
- Upregulation of AT1 receptor pathway (leads to inflammation, fibrosis)
- Downregulation of ACE2/MAS axis (increases inflammation, promotes gut dysbiosis, loss of antimicrobial peptides, abnormal amino acid uptake and metabolism)

