

## Commentary: are blood and saliva sources of COVID-19 spread?

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Recent data indicate that the risk of SARS-CoV-2 spread by blood transfusion is trivial; 0.66% blood donors are SARS-CoV-2 positive in their saliva, and low level of RNAemia is observed in 3.7% of the positive donors<sup>1</sup>. Likewise, although saliva seems to play a role in COVID-19 spreading<sup>1</sup>, this may represent the one-side of the coin.

Saliva is one of the innate defense mechanisms and contains several innate defense agents that exhibit antimicrobial and/or antiviral effects; its lubrication and antibacterial/antiviral properties play a significant role in oral cavity protection. These agents include the so-called antimicrobial peptides [ $\alpha$ - and  $\beta$ -defensins, cathelicidin (IL-37), histatins, statherin], main glycoproteins (mucins, proline-rich proteins, immunoglobulins) and minor glycoproteins (lactoferrin, agglutinin, lysozyme, cystatins)<sup>2,3</sup>. Human  $\alpha$ - and  $\beta$ - defensins 1-4 and IL-37/hCAP-18 possess activities against bacteria, fungi and viruses<sup>4</sup>;  $\beta$ -defensin-4 demonstrates antiviral activities against several respiratory viruses both *in vitro* and *in vivo*, such as influenza A virus H1N1, SARS-COV and MERS-COV<sup>5</sup>. Likewise, human saliva is a rich source of oral epithelial cells that express functional toll-like receptors (TLRs), which are important for initiation of innate immune responses and in the development of adaptive immune responses; TLR agonists exhibit substantial impact on the

inhibition of the genus *Coronavirus* replication<sup>6</sup>. Moreover, both defensins and cathelicidin: a) reduce COVID-19 replication and pro-inflammatory cytokines' levels, which induce inflammatory process that damages the lining of the lungs, resulting in pneumonia, and b) increase anti-inflammatory cytokines' levels. Furthermore, the COVID-19 engineered vaccine structure is adjuvanted by  $\beta$ -3 defensin and included epitopes of helper T-lymphocytes, cytotoxic T-lymphocytes and B-lymphocytes, thereby making the vaccine able to induce a vigorous immune response<sup>7</sup>.

Recent evidence<sup>8</sup> indicates that although hepatitis B virus (HBV) DNA, can be discovered in the saliva of HBV infected patients, it appears unlikely to transmit the infection. As in the case of coronavirus<sup>1</sup>, HBV also exists in many body fluids such as saliva and nasopharyngeal fluid, as measured by qualitative and sensitive PCR methods. The structural protein of HBV appears to contain an RNA-polymerase efficient of forming the adult coronavirus<sup>9</sup>. HBsAg as well as coronaviruses are detected in blood of patients with acute and chronic hepatitis and cirrhosis; electron microscopy studies also revealed cytoplasmic HBsAg and coronaviruses<sup>10</sup>; and cytoplasmic HBsAg fell together to induce membranes of coronavirus<sup>11</sup>.

Since, coronavirus infections are connected with uncontrolled austerity of received measures with negative impact on several human principles

such as personal, social and religious principles, the detection of HBV DNA in saliva motivated our study group to investigate its potential saliva transmission by some hypothetical high risk occupational Greek procedures such as through the Holy Communion Cup. In the first preliminary study included patients from our registry with HBV chronic hepatitis under entecavir<sup>12</sup> and in the next step the relative registry of another Department of the same Hospital was incorporated. Among other parameters studied, the substantial independent categorical variable to evaluate our hypothesis was the patients' occupation, thereby introducing two sub-groups; priests, with a standard active and perpetual weekly exhibition to many people's saliva, and non-priests. The approval by the Institutional Ethics Committee was obtained, and all predispositions of the Helsinki Declaration were fulfilled. The reservoir database did not include any personified information (name, ID number, etc.) and thus no informed consent was necessary. To our knowledge, we reported for the first time in Greece that in the first and second registries (N=71 and 429 respectively) of patients, chronic HBV hepatitis was more frequent among non-priests (98.6% and 99.7%, respectively) compared with priests (1.4% and 0.3%, respectively). Therefore, both of our datasets indicated a decreased prevalence of HBV chronic hepatitis among priests when compared to other occupations, thus possibly indicating that priests appear to be a group that may not commonly be affected by HBV. Similarly, for the first time in Greece, we reported that data from COVID-19 hospitalized patients in a Medical Center of North of Greece, between March 2020 to April 2021, revealed a comparable picture: only 3 from the total 940 (0.32%) COVID-19 inpatients were priests; this parameter is comparable to 0.66% of blood donors observed by others<sup>1</sup>.

Nevertheless, comparable with HBV, further large-scale controlled studies on COVID-19, are mandatory to elucidate in depth these findings, thereby offering significant implications in human life supporting processes, like, among other social encouragement services such as the life-saving blood donation, participation in regular holy services in certain populations accompanied by optimistic psychological impacts on human life, the inhibition of which already fired severe negative economic and psychological impacts (i.e., domestic violence, depression, hopelessness, or suicide) on Geek and international communities. The social, religious, occupational and economic disruption

due to COVID19 has had a negative impact on psychological well-being; and addressing the psychological effects is an essential component of disaster management of infectious pandemics.

#### Conflict of Interest

The Authors declare that they have no conflict of interests.

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