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What's new for the clinician– summaries of recently published papers

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1. Assessing vaccine hesitancy in the population using a generalized vaccine hesitancy survey instrument

From a scientific perspective, the benefits of vaccination have long been demonstrated with rigorous empirical research[1]. To the individual being vaccinated, vaccines provide almost invaluable protection against serious infections, but high coverage levels can also create an additional benefit emerging at the population level. This public good of 'herd immunity', i.e. heavily reduced transmission of a pathogen in the population because of low numbers of susceptible hosts in the population, is an important layer of protection for those individuals who cannot receive vaccination themselves, those with a dysfunctional immune system, and those whose protection has waned.[1] It is mainly for the latter reason that many ethicists believe that vaccination is not merely a matter of personal choice but that it can also be a social obligation.[1]

Despite the demonstrated effectiveness of vaccination programs, there is evidence that in many parts of the world, substantial numbers of people are questioning the need to become vaccinated, seek alternative vaccination schedules, delay or refuse vaccination. The concept of 'vaccine hesitancy' was suggested and defined as broader and less judgmental than skepticism or refusal.[1] So, rather than a set of general anti-vaccine opinions, the concept of vaccine hesitancy is thereby defined as a vaccine and context-specific, behavioral phenomenon that needs to be understood against an expectation of reaching a specific coverage goal, and this under circumstances of sufficient access to vaccination.[1]

Several measurement scales have been developed in order to tap into the core of hesitant vac- cine attitudes. In 2015, the WHO-SAGE Working Group on Vaccine hesitancy developed a scale, called the 'Vaccine Hesitancy Scale' (VHS) that aimed to unify existing research on the many determinants of vaccine hesitancy in a workable framework and to standardize the measurement of vaccine attitude. The VHS allows comparing parental levels of hesitancy across regions as well as to map evolutions of hesitancy over time, and can be linked to socio-demographics in order to identify priority groups.

This study sought to broaden the applicability of the VHS by focusing on vaccine hesitancy within the respondents themselves, rather than an exclusive focus on parental attitudes regarding childhood vac cines. This was done by modifying the perspective and wording adopted in the original VHS, without losing its intended conceptual meaning. Using this revised version of the VHS, the researchers sought to examine vaccine hesitancy among a representative sample of the UK population, and to determine the association between vaccine hesitancy and various respondent characteristics.

METHODS

Using a consumer panel database, 9613 random individuals were approached to participate in a scientific study on healthcare resource allocation. Respondents did not know the specific subject of vaccination before deciding to participate. Of these contacted people, 4144 (43%) responded to the invitation and 1950 were recruited via stratified random selection to fulfill predetermined quotas, which provided a representative sample of the UK population in terms of socio-economic strata (indicated by the occupation of the head of the household), gender and urban vs. rural background. Since the primary interest of this study was related to responses in age groups, a concerted effort was made to recruit individuals equally in 5 age categories (20–29, 30–39, 40–49, 50– 59, 60+ years).

An email containing a link to the survey website was sent to participants and by clicking on the link respondents consented to participate, although they were free to stop or close the survey at any point. All respondents received a nominal incentive for study completion. The vaccine hesitancy scale (VHS) was asked before the start of the resource allocation experiment so no order effects are to be expected.

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Participants were asked to answer ten questions related to their confidence in vaccines on a five point Likert scale (1 = strongly disagree, 2 = disagree, 3 = neither agree nor disagree, 4 agree, 5 = strongly agree). Three questions (five, nine and ten) were phrased negatively. In the original VHS, these ten items were targeted at parents to measure attitude towards childhood vaccination. The researchers modified the 10 items so that they could be asked by anyone without reference to children. For instance, the first item was changed from "Childhood vaccines are important for my child's health" to "Vaccines are important for my health". Respondents were asked various socio-demographic questions such as whether they have or had children (and their age) and they self-rated their health status. In addition, their optimistic or pessimistic expectations about the future were measured via the Revised Life Orientation Test (LOT-R). This is a standard instrument to measure 'dispositional optimism', the relatively stable personality trait of anticipating a good or a bad future.

To study the latent dimensions of the VHS, the dataset was randomly and evenly split into a construction and a validation set. Exploratory factor analysis was conducted on the construction set. Factors were extracted using varimax rotation. Subsequently, a confirmatory factor analysis was used on the validation set to con- firm the latent structure that resulted from the exploratory factor analysis. Simple and multiple regression analyses were used to identify significant associations between the identified VHS sub- scales and hypothesized explanatory variables.

RESULTS

Forty-three percent of the contacted panel members were willing to participate in this study and of these, 1950 were selected based on a number of predetermined quota with 1546 participants completing the questionnaire. When asked how difficult the survey was and whether their answers were sufficiently valid to be used for public policy purposes, 47 (2%) indicated that the survey (which included a discrete choice experiment) "was very difficult and I am not sure that I made a valid contribution". In addition, there were 97 (6.5%) 'straightliners' in the sample, i.e. participants who selected the same response category for each of the 10 items. Sixty-four of them consistently. answered the middle category 'neither agree nor disagree'. These 97 respondents were excluded from the analysis, leaving us 1402 respondents for analysis.

One in five respondents disagreed or were undecided whether "vaccines are effective" (question 2), and two in three respondents did not fully reject the claim that "New vaccines carry more risks than older vaccines" (question 5). Also, for the items "I am concerned about serious adverse effects of vaccines" (question 9) and "Vaccines are not needed for diseases that are not common anymore" (question 10) a majority of respondents answered in a hesitant way. The fraction of respondents that clearly opposed was however much smaller, ranging from 4.4% disagreeing that "vaccines are important for the health of others in my community" to 32.7% stating concerns for side effects. Items 5, 9 and 10 were answered differently compared to the other seven items. These three items showed an even distribution around "neither agree nor disagree" compared to a strongly skewed distribution towards "strongly agree" for the others.

On a scale from 1 to 5 (with 5 maximal hesitancy), the average respondent scored 1.99 (SD = 0.80) for the lack of confidence factor and 2.89 (SD = 0.93) for risks, highlighting that the hesitancy of the average person in our sample was driven more by risk perceptions than by lack of confidence in vaccines.

Using regression analysis for the two VHS subscales, the researchers found several variables that were statistically linked to respondents' answers to the clustered 'lack of confidence' and 'risks perception' items. For the first construct, those aged 50–59 year old showed lower lack of confidence than those aged 20–29 year old. People in rural areas showed higher lack of confidence compared to those from urban areas. Women were more confident than men and, as compared to those without children, parents with children aged >20 years were also less confident. There was no significant association between lack of confidence and employment, education, socio-economic status, health state or optimistic or pessimistic expectations for the future. Regarding the second construct, aversion to the risks of side effects, as compared to those without children, people with young children showed greater aversion to risks. The same can be said for those who were optimistic about their future versus more pessimistic individuals.

CONCLUSIONS

This study found that a a substantial percentage of the British population is vaccine hesitant, these views are not clustered in typical demographic features.

Implications for practice: The important similarities and differences across the different age categories provide evidence of the focus areas needed for education initiatives to increase vaccine uptake levels in populations

Reference

1. Luyten J, Bruyneel L, van Hoek AJ. Assessing vaccine hesitancy in the UK population using a generalized vaccine hesitancy survey instrument. Vaccine 2019; 37: 2494-501.

2. Is there an association between periodontitis and severity of COVID-19 infection?

Most patients with COVID-19 infection usually present with mild symptoms with approximately 14% of confirmed cases developing severe conditions requiring hospitalization and oxygen support, 5% needing admission to intensive care units and around 2% dying.[1] Severe cases are usually complicated by acute respiratory distress syndrome (ARDS), sepsis and septic shock, leading to multi-organ damage and these patients usually have excessive levels of proinflammatory cytokines and widespread tissue damage; the so-called *cytokine storm syndrome*[1]. In fact, COVID-19 mortality has been associated with elevated serum levels of interleukin-6 (IL-6), C Reactive Protein (CRP), D-dimer and ferritin suggesting a clear link between disease severity and a virally driven non-resolving hyperinflammation.

The chronic inflammation associated with severe periodontitis frequently leads to a low degree systemic inflammation and increased levels of cytokines, such as Tumour Necrosis Factor-α (TNF-α), Interleukin (IL)-1β, IL-4, IL-6 and IL-10, as well as CRP and ferritin.[1]

Even though periodontitis and COVID-19 have both been associated with many common comorbidities, there is no evidence of a possible direct association between these two diseases. Marouf and colleagues (2021)[1] reported on a case–control study that sought to estimate the extent to which periodontitis is associated with COVID-19 complications.

METHODS

This study was based in Qatar and every patient with confirmed COVID-19 diagnosis according to the WHO interim guidelines and two subsequent positive PCR test for SARS-CoV-2 were included in a 6 month period from February 2020 to July 2020 provided they mt the following inclusion criteria: - Adults (≥18 years old) discharged or deceased due to COVID-19 before the study end-date (31 August 2020), and with active dental records, with at least one dental appointment during the year preceding the Pandemic (March 2019 to March 2020). Patients with no dental radiographs in the records were excluded because the presence of periodontitis could not be objectively confirmed. Also, patients under the age of 18 were excluded because they are unlikely to develop neither COVID-19 complications nor periodontitis.

This was a case–control study. Cases were defined as patients with registered COVID-19 complications in their records including death, ICU admissions or need of assisted ventilation due to COVID-19. Controls were defined as COVID patients discharged without major complications. No matching for controls was performed as all controls were included for analysis.

The main exposure variable (periodontitis) and covariates (e.g. demographics, medical conditions), and outcomes of COVID-19 were extracted from the electronic health records of included patients. The periodontal status was studied from posterior bitewings and panoramic radiographs in the patient's electronic records, using a dental software program. Interdental bone loss was measured in the posterior sextants using as reference the cement-enamel junction (CEJ) and the total length of the root. The percentage of bone loss was obtained from the most affected tooth using the criteria from the recent classification of periodontal and peri-implant diseases.[1]

Periodontitis was defined when bone loss was detected at two or more non-adjacent teeth, after excluding local factors related to periodontal-endodontic lesions, cracked and fractured roots, caries, restorative factors and impacted third molars. Due to the low sensitivity of panoramic and/or bite wing radiographs for slight bone crestal changes, patients were categorized as follows:

- Periodontally healthy or initial periodontitis (Stages 0–1): Bone loss less than the coronal third of the root length (15%) in OPGs, or ≤2 mm in bitewing radiographs.
- Periodontitis (Stages 2–4): Bone loss more than the coronal third of the root length (>15%) in OPGs, or >2 mm in bitewing radiographs.

Each radiograph was assessed by two blinded investigators. In case of discrepancy, a third blinded investigator reviewed the radiographs, and the majority diagnosis was considered. Information on demographic (sex and age) and other relevant risk factors associated with COVID-19 complications, such as body mass index (BMI, kg/m2), smoking habits, asthma, other chronic respiratory disease, chronic heart disease, diabetes, dermatitis, chronic liver disease, common autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus or psoriasis), solid organ transplant, peptic ulcer, immunosuppressive conditions, cancer, chronic kidney disease, hypertension, cerebrovascular accident, peptic ulcer and deep vein thrombosis were obtained from patient records.

BMI was categorized as overweight/obese (BMI ≥ 25) and adequate/underweight (BMI < 25), smoking was categorized as current/past, and never smokers, and diabetes as present or absent. For the other chronic conditions, we created a variable “comorbidity” by computing the presence of each of the above condition. The values of this variable ranged from 0 to 7; we further categorized the variable according to number of comorbidity into 0, 1, and ≥2 because of low numbers in some of the categories. Blood parameters relevant to the course of the disease such as concentrations of D-Dimer, CRP, HbA1c, Vitamin D, white blood cells (WBC) and lymphocytes were also collected from the electronic records. Both the initial parameters measured upon diagnosis as well as the latest parameters measured prior to discharge were collected.

RESULTS

From the 1076 patients identified with COVID-19 diagnosis and active dental records, 443 were excluded due to either lack of dental radiographs or relevant medical

information. Furthermore, 65 patients were excluded for being <18 years of age. A total of 568 COVID-19 positive patients were included for the analysis. Among these, 40 experienced COVID complications (cases) and 528 were discharged without any complications (controls).

There was an equal sex distribution among COVID 19 patients with and without complications. As expected, patients with COVID-19 complications were older (mean 53.5 vs 41.5) and had more comorbidities than those without any complication. Similarly, more than 80% of all patients who had COVID-19 complications had periodontitis compared to only 43% of those without COVID-19 complications.

A total of 197 patients had laboratory records for HbA1c, 177 for Vit-D, 96 for D-Dimer, 394 for lymphocytes, 397 for WBC and 310 for CRP. Assessment of the latest laboratory records revealed that the concentrations of D-dimer, WBC and CRP were significantly higher in COVID-19-deceased patients when compared with surviving patients. On the other hand, the concentrations of lymphocytes were significantly lower in the deceased patients. Patients admitted to the ICU as well as patients requiring assisted ventilation also had significantly higher D-dimer, WBC and CRP serum levels than patients that did not enter the ICU or those that did not require assisted ventilation, respectively.

Out of the 568 patients included in our study, a 258 presented periodontitis. Among the patients who presented periodontitis, 33 experienced complications, while only 7 of the 310 patients without periodontitis presented COVID-19 complications. The risk of having COVID-19 complications among patients with periodontitis was OR 6.34 (95% CI 2.79–14.61) for any complications, OR 17.5 (95% CI 2.27–134.8) for death, OR 5.57 (95% CI 2.40–12.9) for ICU admission and OR 7.31 (95% CI 2.21–26.3) for need for assisted ventilation. After adjusting for possible confounders such as age, sex, smoking behaviour and comorbidities, the multivariable analysis showed an adjusted OR of 3.67 (95% CI 1.46–9.27) for all COVID-19 complications, 8.81 (95% CI 1.00–77.7) for death, 3.54 (95% CI 1.39–9.05) for ICU admission and 4.57 (95% CI 1.19–17.4) for need of assisted ventilation.

The association between periodontal status and the surrogate laboratory biomarkers studied (HbA1c, WBC and CRP blood levels) were significantly higher in COVID-19 patients with periodontal disease than in those without periodontal disease.

CONCLUSION

Periodontitis was significantly associated with a higher risk of complications from COVID-19, including ICU admission, need for assisted ventilation and death and increased blood levels of markers linked worse COVID-19 outcome such as D-dimer, WBC and CRP.

Implications for practice: This paper provides further evidence of the link between poor oral health and negative general health outcomes for major diseases or infections that affect other parts of the body.

Reference

1. Marouf N, Cai W, Said KN, Daas H, Diab H, Chinta VR, Hssain AA, Nicolau B, Sanz M, Tamimi F. Association between periodontitis and severity of COVID-19 infection: A case–control study. Journal of clinical periodontology. 2021 Apr 1;48(4):483-91.