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Original research

Immunosurveillance associated with upper respiratory symptoms in elite swimmers: The 8-month period leading into Commonwealth Games

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ABSTRACT

Objectives: To monitor individual mucosal immunity and identify potential risk factors of upper respiratory symptoms in elite swimmers over a competitive season.
Design: Eight-month longitudinal study, observing mucosal immunity, Epstein–Barr virus status, training loads and illness symptoms of elite international swimmers, leading into the Commonwealth Games 2018.
Methods: Participants were fourteen elite swimmers (age ± standard deviation = 19.9 ± 0.8 years, height = 178.9 ± 6.3 cm, and mass = 75.0 ± 7.7 kg). Self-reported upper respiratory symptoms, training load and saliva samples were collected weekly. Venous blood samples were taken at study commencement to determine Epstein–Barr virus status.
Results: Throughout the study, 70 episodes of upper respiratory symptoms were recorded resulting in 34 days of missed training. Incidence ($p = 0.001$), severity ($p = 0.022$), and duration of upper respiratory symptoms ($p = 0.001$) were significantly higher during high training loads, compared to low. Eight swimmers (61 %) had evidence of past infection with Epstein–Barr virus, but this had no relationship with incidence, severity, or duration of upper respiratory symptoms ($p > 0.05$). Relative individual salivary immunoglobulin A concentration was 12 % lower when upper respiratory symptoms were present but was not statistically significant ($p = 0.101$).
Conclusions: This study highlights the importance of individual athlete monitoring, to identify swimmers at increased illness risk. Identification of possible risk factors for upper respiratory symptoms, such as increased training load, may allow for modifications in training or other illness preventative strategies for elite swimmers.

Practical implications

- Findings support the use of individual monitoring of self-reported URS and sIgA, specifically exploring individual trends over time.
- Absolute sIgA was significantly lower on weeks where URS were reported and following the trend of relative sIgA leading into URS, could provide support to the use of sIgA in athlete monitoring for athletes and physiologists.
- Coaches should consider reductions in training load for athletes who present frequent URS, to promote increased performance and athletic success. For those at heightened risk of URS, small reductions in training load would outweigh the negative impact that increased URS and subsequent missed training could have.

1. Introduction

The majority of research suggests that a greater degree of immune suppression and increased risk of illness occur during winter and during the heaviest training periods.[1,2] International swimming events such as the British Swimming Championships or the Commonwealth Games usually fall in April, meaning that high volumes and intensity of training occur throughout winter months, which would further accentuate risk of illness. In order to compete successfully at an elite level, high training loads are necessary; however, this often coincides with greater illness symptoms which negatively affect athletes' ability to train and subsequently perform.[3]

Immunoglobulin A is the most prominent protein within mucosal secretions[4] and plays a vital role in innate immune response.[5] Salivary immunoglobulin A (sIgA) has become a meaningful biomarker of mucosal immunity; specifically, several studies in swimmers have highlighted an association with depressed sIgA and increased incidence of upper respiratory illness (URI).[2] Despite some conflict,[6] a recent systematic

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review examined 23 studies and confirmed that low sIgA (concentration and secretion rates) was correlated with higher incidence of URI.[7] Mixed findings may be reflective of the large within- and between-subject variation found with sIgA. Specifically, within-subject variability seen in elite athletes indicates that some athletes are more susceptible to illness than others,[8] explaining the need to monitor changes in sIgA in individual athletes rather than comparing group means.[9]

Given the complexity and highly individualised nature of mucosal immunity and URI, it could be argued as inappropriate to compare groups and mean data. This is because marginal, yet important physiological changes would not necessarily be revealed amongst individual athletes. Longitudinal monitoring of illness, sleep, injury, training, and many other physiological and psychological parameters in elite athletes has been widely investigated[10]; therefore, an individualised approach can be regarded as more appropriate to detect the marginal changes that can strongly influence an athlete's ability to train and perform optimally. Moreover, the sample size availability of elite athletes is limited and therefore lends itself more to monitoring changes in individual athletes as opposed to cohort and group data tracking.[11] With this, individual athlete monitoring could help identify those at risk of frequent URS, to adopt preventative strategies, including training and lifestyle modifications for optimal training and performance.[9] Taken together, the importance of monitoring athletes independently of one another is evident.

Due to the uncertainty regarding the aetiology of upper respiratory illness and the inability to clinically determine causes, it has been favoured to report URS instead of URI or URTI.[12] This is important because overall, the major concern for coaches and athletes is the accompanying illness symptoms that can limit training and prevent successful competition.[13] Therefore, it was suggested further study would be required to uncover causes of unidentified URS and risk factors in athletes.[14] Epstein–Barr virus was identified as one of the most likely causes of URS,[13] suggesting viral reactivation rather than primary infection. Specifically, a significant relationship between EBV seropositivity and URS was reported for swimmers.[15] Therefore, the aims of the current study were to explore an individualised approach to monitoring changes in mucosal immunity in elite swimmers, in relation to EBV serostatus and other potential risk factors for URS.

2. Methods

Twenty-three elite international swimmers were recruited, from Loughborough University Performance squads. Nine athletes did not complete the study; five did not train on the chosen analysis day due to university commitments, and four retired before the commencement of the study. Therefore, fourteen elite athletes were included in the observational study (age ± SD = 19.9 ± 0.8 years, height = 178.9 ± 6.3 cm, and mass = 75.0 ± 7.7 kg). The current study investigated two different training groups: the sprint group (female, n = 4; male, n = 2) and the middle-distance/distance group (female, n = 1; male, n = 7). Prior to study commencement, swimmers provided fully informed consent and completed health screens. The right to withdraw at any time and confidentiality were assured, through use of codification for analysis. Ethical approval was granted for human investigation by The University of Hertfordshire, Health Science Engineering & Technology ECDA (ethics protocol number: aLMS/PGR/UH/02940(1,2,3)).

Elite swimmers were observed for 8-months leading into an international meet; either the Commonwealth Games 2018 (5–10th April) or Swim Cup Eindhoven (13–15th April). Before the commencement of the study, height, body mass, blood and saliva samples were taken for baseline measurements. Whole venous blood samples were collected from consenting athletes (n = 13) by standard venepuncture, from an antecubital vein. Blood samples were used for the detection of IgM and IgG antibodies for the EBV viral-capsid antigen (VCA) and IgG antibodies for the EBV nuclear antigen (EBNA), which was completed by three separate Human ELISA kits (ab108730, ab108731, ab108732; AbCam, Cambridge, UK). Intra-assay coefficient of variation (CV) was 2 % for triplicate samples.

Unstimulated saliva was collected using a passive drool method by tilting the head forwards and drooling into a collection tube (at least 30 min after eating, drinking, or tooth brushing). Saliva samples were collected weekly over the 8-month period in standardised conditions, every Wednesday at 12:00 h to control for effects known to alter sIgA. Athletes were asked to passively drool for 3 min; however, if insufficient saliva was collected, participants were asked to drool for an extra 2 min and record total time. The saliva flow rate ($mL \cdot min^{-1}$) was calculated by dividing the volume of saliva by the collection time; the density of saliva was assumed to be 1.0 $g \cdot mL^{-1}$.[16] Secretion rate ($\mu g \cdot min^{-1}$) of sIgA was then determined by multiplying IgA concentration by the saliva flow rate.[17] All samples were double centrifuged at 4000 RPM for 10 min (Sorvall ST 8R, Thermo Fisher Scientific, USA) to remove supernatant, then divided into four aliquots and stored at −80 °C until analysis. Saliva was analysed on a commercially available Secretory IgA ELISA Kit (1-1602; Salimetrics LLC, Irvine, CA). Inter-assay CV was 8 % and intra-assay CV was 2 % for duplicate samples.

Swimmers were observed for 8 months using weekly reporting of training and illness symptoms using an adaption of the Australian Institute of Sport (AIS) monthly illness log.[18] The type, severity, and duration of illness symptoms were calculated using data collected from the questionnaires. The presence of perceived weekly symptoms was recorded according to their type and severity (1 = no change in training programme, 2 = training programme modified, 3 = complete cessation of training). An episode of URS was defined as reporting URS on 2 or more consecutive days, or when the severity was rated highly enough to modify training (moderate–severe).[18] For any subsequent episode of URS to be classified as a new episode, there needed to be an asymptomatic period of ≥7 days.[14]

Periodised training plans were provided by Loughborough swim coaches, which highlighted the training load for each week and were classified as low, moderate, and high. This was additionally observed alongside the athletes' weekly session ratings of perceived exertion (RPE); individual athlete training load was examined by multiplying the perceived intensity of swim training by the distance swum (km) that week.

All data was compiled using Microsoft Excel and evaluated using both SPSS software (v26.0; SPSS Lead Technologies Inc., Chicago, IL) and GraphPad Prism 8.0 (GraphPad Software, Inc., San Diego, CA). All results are presented as mean ± SD, and significance was accepted at the p ≤ 0.05 level. Partial eta-squared ($\eta^2_{partial}$) was used to report effect sizes for ANOVA where effects were classified as small (0.01–0.08), moderate (0.09–0.25) and large (>0.25).[19]

3. Results

Over the course of the 8-month observation, 70 episodes of URS were recorded for all swimmers. An average of five episodes of URS (median: 5) was reported for each swimmer, ranging from zero (n = 1), to eight reported episodes. A significantly higher number of episodes (60 %) were reported by swimmers during high training load, compared to low and moderate training loads ($p = 0.001$, $\eta^2_{partial} = 0.602$). Average duration for an episode of URS was eight days (median: 7) for all swimmers (range 2–28 days). Average duration of symptoms was 2 ± 3, 7 ± 5, and 9 ± 4 days for low, moderate, and high training loads respectively, showing significantly longer symptom duration during moderate and high training loads compared to low ($p = 0.001$, $\eta^2_{partial} = 0.523$). Over the observed period, the symptom severity score ranged from 2 to 63; a significantly higher symptom severity score was reported during high training loads (15 ± 9), compared to low (3 ± 4) ($p = 0.022$, $\eta^2_{partial} = 0.294$). There were 34 days of missed training due to reported URS, from nine swimmers (range 1–11 days for each swimmer). Despite lacking statistical difference between training loads ($p = 0.83$), 76 % of missed training days due to URS were during high training loads.

Table 1
Illness parameters and sIgA over different training loads between sexes.

Training load	Sex	Episodes of URS	Symptom severity score	Average duration of URS	IgA concentration ($\mu g \cdot mL^{-1}$)	IgA secretion[b] ($\mu g \cdot min^{-1}$)	Saliva flow rate ($mL \cdot min^{-1}$)
Low	Male	6	4 ± 4	5 ± 3	163 ± 47	167 ± 69	0.99 ± 0.21
	Female	3	3 ± 3	3 ± 0	223 ± 121	138 ± 62	0.66 ± 0.11
Moderate	Male	11	4 ± 6[a]	9 ± 4	216 ± 123	178 ± 77	0.93 ± 0.21
	Female	8	19 ± 16	9 ± 4	196 ± 86	124 ± 43	0.70 ± 0.06
High	Male	26	15 ± 10	10 ± 4	194 ± 103	175 ± 68	0.98 ± 0.20
	Female	16	14 ± 6	9 ± 2	187 ± 90	114 ± 41	0.65 ± 0.10

Note. Illness parameters and measurements of sIgA for male (n = 9) and female (n = 5) swimmers. Data is shown as mean ± SD.
[a] Significance for symptom severity score between sexes, during moderate training loads.
[b] Significant main effect was found for IgA secretion between sexes.

Over the 8-month study, mean sIgA concentration was 204 ± 147 $\mu g \cdot mL^{-1}$. Salivary IgA was variable within-subjects, with a mean CV of 33 %. The difference in the mean value between the lowest and highest individual sIgA concentrations, was almost 29-fold (31 $\mu g \cdot mL^{-1}$ vs. 892 $\mu g \cdot mL^{-1}$), and the between-subject CV was 72 %. Despite this variation, absolute sIgA concentration was significantly lower on weeks where swimmers reported URS, compared to weeks they did not ($Z = 2.132$, $p = 0.033$). However, no differences were found for saliva flow rate ($Z = 1.364$, $p = 0.172$) or sIgA secretion rate ($Z = 0.874$, $p = 0.382$). No interaction was found between training loads for sIgA concentration ($p = 0.530$) or sIgA secretion rate ($p = 0.632$). Overall, female swimmers had significantly less sIgA secretion than men ($p = 0.045$, $\eta^2_{partial} = 0.228$). Differences between sexes over differing training loads for all URS parameters were also examined (Table 1). Mixed model ANOVA found significantly higher symptom severity for female swimmers than male, during moderate training loads ($p = 0.030$, $\eta^2_{partial} = 0.254$).

When sIgA values were normalised to each individual's mean, relative sIgA concentration was 12 % lower during URS than when there were no symptoms present (Fig. 1). Relative sIgA concentrations before, during, and after URS were compared with repeated measures ANOVA (Greenhouse–Geisser correction) and no significance was found ($p = 0.101$, $\eta^2_{partial} = 0.360$).

When examining deviation from an individual's average healthy sIgA concentration, 13 out of 14 swimmers spent 50 % or more time below this over the whole 8-month season. On average, swimmers spent 58 % of the season being below their average healthy sIgA concentration; one swimmer spent 71 % below average and reported above average URS episodes (total of 6) (Fig. 2). Additionally, 10 out of 14 swimmers were above their individual healthy average sIgA concentration during and up to two weeks after competition (weeks 16 and 32).

Eight swimmers had evidence of past infection with EBV (61 %, 95 % CI [0.32, 0.86]). Five out of the eight seropositive swimmers (63 %, 95 % CI [0.24, 0.91]) showed presence of antibodies for Epstein–Barr nuclear antigen (EBNA). No swimmer had detectable levels of anti-viral capsid antigen (VCA) IgM antibodies in their serum, indicating none had current EBV infection prior to the commencement of the study. The serology status of EBV was compared against self-reported symptoms, however, no differences were found between EBV serostatus and any of the variables ($p > 0.05$). It would be important to note that although findings were non-significant, those who were EBV seropositive reported a higher number of URS episodes (43 vs 27, $p = 0.170$), missed training days (25 vs 9, $p = 0.128$), and higher symptom severity score (63 vs 45, $p = 0.953$).

4. Discussion

The current study was designed to explore an individualised approach to monitoring changes in mucosal immunity, in relation to EBV serostatus

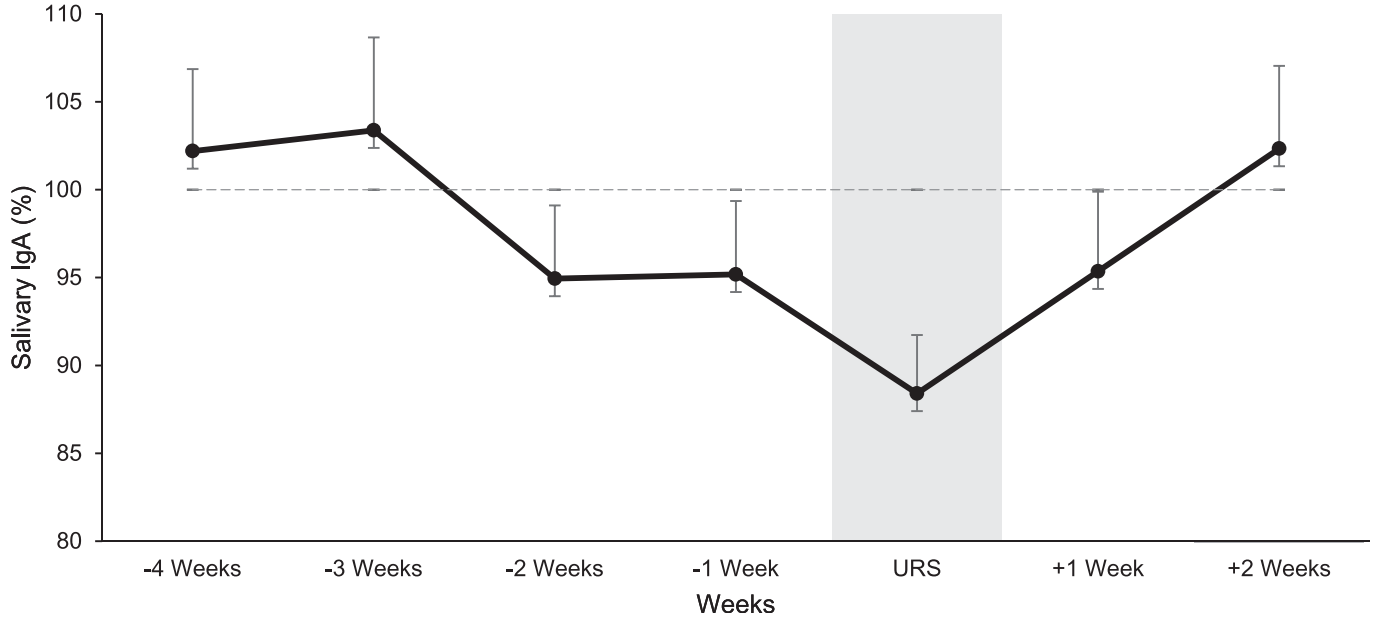

Fig. 1. Seven weeks of salivary IgA (%), leading in and out of episodes of URS.
Note. Average relative sIgA (%) plotted over 7 weeks for all feasible URS episodes. Salivary IgA was normalised by each individual's mean; data presents 4 weeks before an episode of URS, then 2 weeks after (n = 59).

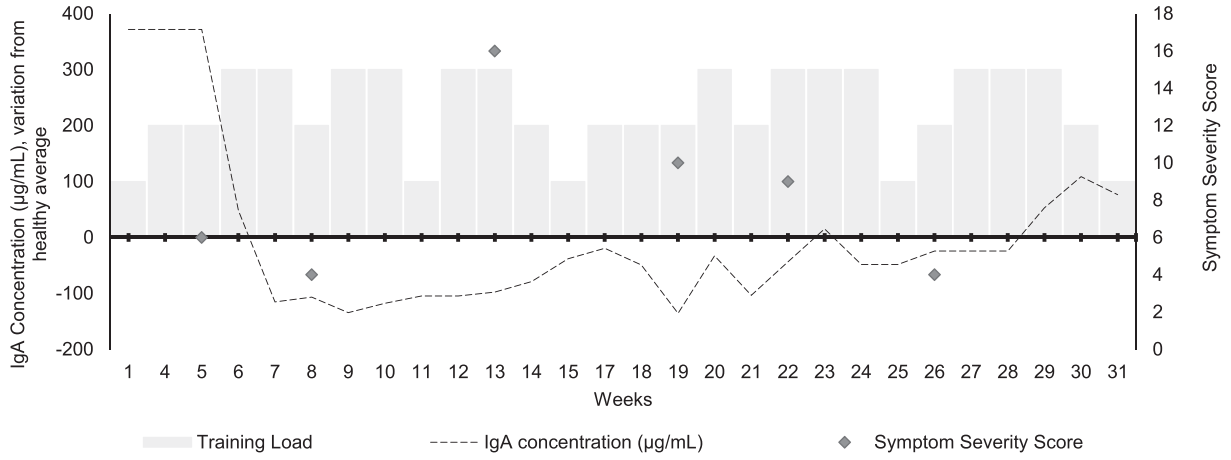

Fig. 2. Variation from the average IgA concentration, plotted over the 8-month season for one swimmer.
Note. This data shows the swimmer spending 71 % of the season, under their reported average (n = 1).

in elite swimmers, as opposed to cohort and group comparisons. Alongside this, the effect of training load and EBV serostatus was examined in regard to URS and sIgA, over an 8-month season. Firstly, it was found that higher training loads, increased the number of episodes of URS, sympom severity, and duration. Absolute sIgA concentration was significantly lower on weeks where URS were reported but displayed no change between training loads. Following the trend of data, it may also be possible to use relative sIgA as a predictor of URS in elite swimmers. Results showed no significant relationship between EBV serostatus and URS. However, upon reflection of the findings, it could be argued that the sample size was too small and therefore, requires further exploration.

With an average of five episodes of URS in the 8-month study, current swimmers had higher incidence of URS than that of the general population (3 episodes)[20] and was in line with other studies conducted on athletes (2–5 episodes).[21] Furthermore, significantly more episodes of URS, a higher symptom severity score, and longer duration of URS, were reported during high training loads. In support, other literature has found most URS to occur during the heaviest training periods.[1,14] One study monitored 19 elite swimmers for 7 months in winter, recorded daily illness symptoms and found that 67 % occurred around high-volume training loads.[1] Interestingly, their non-athletic controls did not show similar URS occurrence at the same time points, suggesting the high training loads to be a causal factor for illness.[1] Due to no control group, the current study cannot comment on this; however, lowered immunity and increased rate of illness have been repeatedly shown in elite athletes, following high intensity training bouts.[14,21,22] Therefore, these findings strengthen and highlight the issue of increased risk of URS, duration, and severity during intense training periods.

Missed training days due to illness was an issue for some swimmers, particularly in the high training load phases. One study identified that athletes were seven times more likely to achieve a performance goal if they completed >80 % of planned training weeks, plus performance success significantly reduced for every week of missed training.[23] Interestingly, there was no significant difference in the number of episodes of URS between low and moderate training loads. Although high training loads are needed for physiological adaption to occur, for those at heightened risk of URS, small reductions in training load may outweigh the negative impact that increased episodes of URS and subsequent missed training could have.

Even with large variation, absolute sIgA concentration was significantly lower on weeks where swimmers reported URS, which has similarly been shown for rugby players.[24] Regarding sIgA secretion rate, no relationship was identified for reported URS vs. non-URS weeks. Conversely, one study found that participants suffering with URS had significantly lower sIgA secretion rate and saliva flow rate, but not sIgA concentration, when compared to illness-free participants.[25] However, the lack of studies investigating this relationship makes conclusions difficult. A significant effect was found for sIgA between sexes, with females showing a significantly lower sIgA secretion rate than men. These findings are supported elsewhere,[26] and could be explained by females having lower unstimulated saliva flow rates compared to men because of smaller salivary glands.[27]

Despite strict controls, there was high within- and between-subject variability of sIgA concentration which highlighted the complex nature of mucosal immunity.[8] Differences in study design, sporting population, level of fitness, saliva collection methods, and large between-subject variability of sIgA, provides a feasible explanation for the vast differences in findings for sIgA between studies. Because of this, authors have suggested sIgA lacks reproducibility, and sensitivity for the detection of illness susceptibility.[4] However, in the current study, significantly lower sIgA concentrations were reported for weeks that swimmers reported URS. This strengthens the potential for use of sIgA as a biomarker of mucosal monitoring for athletes. It should be considered that instead of direct comparisons between studies and comparing groups, individual sIgA monitoring should be used as an in-house tool by coaches and physiologists. This suggestion is supported by the complexities of mucosal immunity; individual monitoring can be considered more appropriate to detect the marginal changes in sIgA, in addition to lending itself better to longitudinal data monitoring which is typically gathered by coaches and physiologists from elite athletes.

Interestingly, when observing all feasible URS episodes over all seven time points, relative sIgA could be seen going below an individual's healthy average two weeks prior to URS and was 12 % lower during URS. Therefore, following the trend of the graph, it may be possible to use relative sIgA as a predictor of URS in elite swimmers, which aligns with another longitudinal study.[8] Due to infection incubation time being usually shorter than one week, researchers postulated that the reduction in sIgA in the weeks prior to illness was a contributing factor to URS.[8] With use of individual monitoring, it could help identify those at increased risk of recurrent episodes of URS. As an example, one swimmer spent 71 % below their individual healthy average and reported above average episodes of URS (total of 6) over the testing period. High between-subject variability of absolute sIgA is indicative of the high complexity of mucosal immunity. Therefore, it would be pertinent for coaches and sports scientists to take an individualised approach to managing swimmers' training and competition schedules, whilst using a physiological biomarker and subjective data to inform their decisions. The data presented here shows the novelty of the current study and supports individual athlete monitoring which could be linked back to performance metrics.

To the investigator's knowledge, this was the first study in the UK to examine EBV serostatus in elite international swimmers. More than half of the swimmers in the current study, had previous infection with EBV. The level of EBV seropositivity in the current cohort of swimmers (61 %) was lower than that of previous investigations of elite swimmers (79 %)[15] and University athletes (84 %).[28] However, a larger study conducted on 274 national-level young athletes from 10 different sports, also reported 60 % of athletes to be EBV seropositive.[29] These findings are important because prior EBV infection has been associated with increased URS risk in athletes.[15]

That said, no significant differences for the number of episodes of URS, symptom severity score or duration of episodes were found between EBV serostatus. In support, other research found that susceptibility to illness was not associated with EBV seropositivity.[29] These findings question the validity of monitoring EBV status, as a risk factor for URS in athletes. That said, it should be considered that current results may not have been statistically significant due to the small sample size. Despite lack of significance, those who were EBV seropositive reported a higher number of URS episodes, symptom severity score and missed training days.

Although statistical power was achieved for other variables, a limitation of the current study would be the small sample size when grouping swimmers, either by training group, sex, or EBV serostatus. There is ongoing debate within sport science research when conducted in elite athletes, as high numbers of participants are needed to provide sufficient statistical power. Pre-study power calculations are often unrealistic when recruiting elite athletes.[11] Although lacking statistical significance, a large effect size was found for relative sIgA concentrations before, during and after URS. Perhaps this large effect size may be more relevant when presenting findings and trying to draw conclusions with smaller populations. Therefore, individual data and trends could be more useful to coaches and researchers in elite sport, compared to analysing differences between group statistical data and p values. Lastly, it should be considered that other aspects not controlled in this investigation, could also play an important role in the complex relationship between training and mucosal immunity. These could include nutritional status, sleep, and the fact that the swimmers were university students potentially cohabiting together, with additional stressors.

5. Conclusion

The current study presented a well-controlled, longitudinal observation of mucosal monitoring alongside risk factors associated with URS, in elite international swimmers. Current study findings promote the use of monitoring individual changes in mucosal immunity, rather than cohort and group analysis. Absolute sIgA was significantly lower on weeks where URS were reported and following the trend of relative sIgA leading into URS, could provide support to the use of sIgA in athlete monitoring. Here, EBV serostatus had no relationship with URS, however data was inconclusive due to small sample size and warrants further investigation. Findings additionally strengthen the notion that high training loads present an increased number of episodes of URS, symptom severity, and duration. The importance to further improve illness monitoring practices in elite swimmers is evident, as moving forward it may allow for modifications in training or other protective strategies.

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Confirmation of ethical compliance

Athletes received written and verbal instructions via an information sheet, about what the longitudinal study would entail and were made aware of the risks and benefits of participating. Prior to study commencement, participants provided fully informed consent and completed health screens. They were given the right to withdraw at any time and confidentiality was assured, through use of codification for analysis. Ethical approval was granted for human investigation by The University of Hertfordshire, Health Science Engineering & Technology ECDA (ethics protocol number: aLMS/PGR/UH/02940(1,2,3)).

CRediT authorship contribution statement

Lauren H. Baker: Conceptualization, Methodology, Formal Analysis, Investigation, Resources, Writing- Original Draft. **Terun Desai:** Investigation, Writing- Review and editing, Supervision. **Mark Green:** Writing- Review and editing, Supervision. **Amy V. Wells:** Conceptualisation, Writing- Review and editing, Supervision.

Declaration of interest statement

None.

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