

# METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* AND ITS CURRENT SCENARIO IN NEPAL - A BRIEF REVIEW

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## ABSTRACT

*Staphylococcus aureus* is one of the species of gram-positive cocci arranged in cluster belonging to family *Staphylococcaceae* under which there are at least 40 species. It is non-spore forming, non-motile, facultative anaerobic, catalase positive, producing 'golden yellow' pigment and can grow in 10.0% sodium chloride. *S. aureus* is responsible for causing infections ranging from minor skin infections such as boils, impetigo to fatal necrotizing infections such as pneumonia, surgical site infection, necrotizing fasciitis, bacteremia with possible complications of endocarditis or severe sepsis infections. Methicillin, a semisynthetic and narrow-spectrum penicillin-derived drug, was introduced to treat penicillin-resistant *S. aureus* infection in 1959, however, just after one year of its introduction, it developed resistance in England in 1960. Methicillin resistant *S. aureus* (MRSA) has now been reported all over the world. The first case of MRSA from Nepal was reported in 1990. Since then, many reports from different parts of Nepal have been reported some of them have also been confirmed by the detection of *mecA* gene. Coming to this point, this bacteria has developed resistance against various antibiotics and are termed as multidrug-resistance (MDR) making hard or impossible to treat its infections. MRSA has also been detected in among health care workers as well as inanimate materials and some animals. It is, therefore, important to implement the effective antibiotic policy along with regular surveillance of MRSA and VRSA is essential to contain MRSA infections.

## KEYWORDS

MDR, MRSA, Nepal, worldwide, *Staphylococcus aureus*,

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## STAPHYLOCOCCUS: INTRODUCTION

*Staphylococcus aureus* are one of the species of gram-positive cocci arranged in cluster belonging to family *Staphylococcaceae*. They are non-spore forming, non-motile, catalase-positive, facultative anaerobes that produce 'golden yellow' pigment and can grow in 10.0% sodium chloride. Under this family, there are at least 40 species of staphylococci recognized by biochemical and nucleic acids analysis.<sup>1-3</sup> Of these, some species are present in human as significant part of body's normal microbiota such as *S. aureus* (in nares) and coagulase-negative *Staphylococcus* spp. (CONS), i.e. *S. epidermidis* (mainly in skin), *S. saprophyticus* (occasionally in skin); and *S. haemolyticus*, *S. cohnii* and *S. warneri* (in skin).<sup>1</sup> However, they harbour substantial pathogenic potential with *S. aureus*, *S. epidermidis* and *S. saprophyticus* as the most commonly encountered species as human pathogens and their key identification characters shown in Table-1.<sup>4</sup>

respectively. Very recently (in 2025), Jiang *et al*<sup>20</sup> reported on the spread of the "agrA-I238K ST5 MRSA clone" across East and Southeast Asia. Because of spread of infection with MRSA - "the super bug" and high morbidity as well as mortality, October 2 has been declared as MRSA day. These days, MRSA according to its origin, has been divided into three types such as (i) healthcare associated MRSA, (ii) community associated MRSA and (iii) livestock associated MRSA.<sup>17</sup> Given its health impact, WHO has listed MRSA as high priority bacterial pathogen in 2024.<sup>21</sup>

### Nepalese scenario

**MRSA in clinical samples:** In 1987, methicillin resistance was reported for the first time from Nepal by Rai *et al* (1987)<sup>22</sup> in CONS isolates. Three years later, in 1990, Rai *et al*<sup>23</sup> reported MRSA for the first time in Nepal among patients, staffs and hospital environment. Since then, many reports on MRSA have been published from Nepal. As reviewed by Khanal *et al*<sup>24</sup> over 25 reports are available only after

**Table 1: Differentiation of *S. aureus*, *S. epidermidis* and *S. saprophyticus* (Reynolds, 2021)<sup>4</sup>**

| Characteristics                   | <i>S. aureus</i> | <i>S. epidermidis</i> | <i>S. saprophyticus</i> |
|-----------------------------------|------------------|-----------------------|-------------------------|
| Pigment production (on SM110)     | Usually golden   | Usually white         | Usually white           |
| Coagulase reaction                | +                | -                     | -                       |
| Alpha toxin ( $\beta$ -hemolysis) | +                | -                     | -                       |
| Acid from mannitol                | +                | -                     | +                       |
| DNase production                  | +                | -                     | -                       |
| Sensitivity to novobiocin         | Sensitive        | Sensitive             | Resistant               |

Of these species, *S. aureus* is responsible for causing infections ranging from minor skin infections including impetigo, boils, cellulitis, folliculitis, abscesses to surgical site infection, pneumonia, necrotizing fasciitis, bloodstream infections including endocarditis and even the fatal sepsis.<sup>1,3,5</sup> *S. aureus*, particularly the methicillin-resistant *S. aureus* (MRSA), is a well-established nosocomial pathogen.<sup>6-9</sup>

**Emergence of methicillin resistant *S. aureus* (MRSA):** In 1959, methicillin, a semisynthetic and narrow-spectrum penicillin-derived drug, was introduced to treat penicillin-resistant *S. aureus* infection. However, just after one year of its introduction, i.e. in 1960, Patricia Jevons<sup>10</sup> detected MRSA in England. According to MRSA Action UK,<sup>11</sup> the first case of MRSA in USA was reported in Boston in 1968. Since then, the cases of both healthcare- and community-acquired MRSA infection are increasing rapidly.<sup>12</sup> According to a review article including 119

studies from 29 countries, the pooled global prevalence of MRSA was reported to be 14.69%.<sup>13</sup> Another review article by Zhou *et al*<sup>14</sup> noted the overall prevalence of MRSA in patients with diabetic foot ulcer as 17.0%. According to Encyclopedia Britannica,<sup>15</sup> globally, MRSA has been found to be responsible for more than 100,000 deaths in 2019 and an estimated two in every 100 people harbor MRSA.

Methicillin resistance in *S. aureus* occurs due to the acquisition (presence) of the *mecA* and *mecC* genes which are associated with modification of penicillin-binding proteins that has reduced  $\beta$ -lactam affinity, thus, limiting antimicrobial effectiveness.<sup>16-19</sup> According to a meta-analysis by Suleiman *et al*,<sup>19</sup> the current global prevalence of MRSA based on detection of *mecA* / *mecC* positivity ranges from 0.90 % to 69.98 % with an average prevalence of *mecA*-positive human MRSA, animal MRSA and worldwide MRSA as 21.8 %, 7.1 % and 14.58 %, respectively.

2008 with the prevalence of MRSA ranging from 14.6% to 72.4% with a pooled prevalence of 38.2%. They noted that, at national level, the prevalence was about 46.0% during the year 2003-2009, which decreased during 2009-2015 and increased during 2015-2019 indicating an increasing trend of MRSA infections during recent years. The highest MRSA prevalence was found in Gandaki Province (53.6%) and lowest in Bagmati Province (33.2%). In addition, they noted no significant temporal variance in MRSA infection rate in Kathmandu Valley. Another review article by Shrestha *et al*<sup>25</sup> mention that *S. aureus* among clinical isolates in Nepal is 34.5% of them an average of 57.1% is multi-drug resistant (MDR). MRSA accounted for a total of 41.7% and inducible clindamycin resistance was detected in about 35.0% of the isolates.

Subedi and Brahmadathan<sup>26</sup> reported the MRSA prevalence of 15.4% among the *S. aureus* isolates from clinical samples at tertiary care center in Pokhara as detected by disc diffusion method. Kumari *et al*<sup>27</sup> reported the 26.1% prevalence of MRSA at a tertiary care center in Dharan by disc diffusion method and majority of the isolates were from pus and wound swabs. Inpatient department was the predominant source with 70.0% prevalence and more than 65.0% of the isolates were multi-drug resistant (MDR). Thapa *et al*<sup>28</sup> reported MRSA prevalence of 29.2% among *S. aureus* isolated from pediatric patients at a Children's Hospital in Kathmandu. Tiwari *et al*<sup>29</sup> reported the MRSA prevalence of 69.1% (112/162) at a tertiary care center in Bhairahawa as detected by disc diffusion method in which hospital-acquired MRSA was higher than community-acquired. Of the MRSA strains, 40.1% were MDR. Khanal and Jha<sup>30</sup> have reported relatively high prevalence of MRSA (68.0%) among patients with skin infection in Chitwan. Ethnically *Tibeto-Burmans* had higher MRSA infection rate (72.5%) than *Indo-Aryans* (56.8%) with significantly higher among males than in females. isolated were MRSA and all of them were MDR. Whereas, the prevalence of antiseptic resistance gene such as *qacA/B* was 48.0% and *smr* was 64.0%. Sapkota *et al*<sup>31</sup> reported MRSA in 31.1% (82/264) clinical isolates isolated from clinical samples in Kathmandu as detected by disc diffusion method. The MRSA was higher among in-patients (46.5%) compared to outpatient 25.4%.

Kattel *et al*<sup>32</sup> reported the MRSA prevalence of 43.5% among the *S. aureus* isolates isolated from urine sample at tertiary care hospital in Kathmandu as detected by disc diffusion (oxacillin and cefoxitin) method. Almost similar findings (42.4%) has been reported by Mishra

*et al*<sup>33</sup> at the same hospital and most of MRSA were MDR. Shrestha *et al*<sup>34</sup> reported MRSA prevalence of 52.9% among *S. aureus* isolates at hospitals based in Kathmandu and Lalitpur as detected by disc diffusion method and most of them were MDR. Ansari *et al*<sup>35</sup> reported a MRSA prevalence rate of 43.1% among the *S. aureus* isolates isolated a tertiary care center in Chitwan as detected by cefoxitin and oxacillin disc diffusion test. One year later, however, same group<sup>36</sup> reported the relatively lower prevalence of MRSA (34.8%) in *S. aureus* isolated from pyogenic infection of skin, soft tissue and bone. Bhatta *et al*<sup>36</sup> reported MRSA prevalence of 34.7% among 400 *S. aureus* isolates isolated from clinical samples. MRSA was detected by cefoxitin and oxacillin disc diffusion method and MRSA were higher in patient department isolates compared to outpatient department isolates. Majority of MRSA (73.4%) isolates were multidrug resistant. However, Khanal *et al*<sup>38</sup> reported a low MRSA prevalence (21.1%) at a tertiary care center in Kathmandu by disc diffusion method. In another study done by Adhikari *et al*<sup>39</sup> in Chitwan MRSA was found to be only 17.1% and all of them were MDR. However, Kadariya *et al*<sup>40</sup> reported even lower rate of MRSA in Nepal (5.8%) as well as Bhutanese refugees living Northeast Ohio, USA (1.1%). Of them, MDR was higher (44.2%) in Nepal compared in NEO (23.9%). On the other hand, Sapkota *et al*<sup>41</sup> reported MRSA in 70.6% of *S. aureus* isolated from clinical samples as detected by disc diffusion method. A study done by Adhikari *et al*<sup>42</sup> in Kathmandu found the prevalence of MRSA to be 26.4% and most of them were isolated from pus sample and all MRSA were MDR. Rajbhadari *et al*<sup>43</sup> reported the MRSA prevalence rate of 45.1% in three years (2021-2023) period at Patan Hospital in Kathmandu Valley. Very recently, Khanal *et al*<sup>44</sup> have also reported that 40.0% of *Staphylococci* isolated from hospital surveillance swabs and all of them were MDR.

Pradhan *et al*<sup>45</sup> reported MRSA prevalence of 57.0% among 1,804 *S. aureus* infected patients at Patan Hospital and in the three years study (2018-2020), MRSA prevalence was higher in 2019. Maharjan *et al*<sup>46</sup> reported MRSA prevalence of 60.8% among *S. aureus* isolates isolated from in Kathmandu by cefoxitin disc diffusion method whereas 11.1% were vancomycin resistant (VRSA) and 40.0% of VRSA were positive for *vanA* gene. At a tertiary care center in Eastern Nepal, Shah *et al*<sup>47</sup> reported MRSA prevalence of 62.1% of *S. aureus* isolates as detected by cefoxitin disc diffusion method whereas the MRSA prevalence among community acquired infections and hospital acquired infections

was 55.4% and 44.6%, respectively. However, none of the *S. aureus* isolates were resistant to linezolid. Neupane *et al*<sup>48</sup> from KIST Teaching Hospital in Kathmandu reported 61.3% MRSA as detected by disc diffusion method out of which 67.3% were MDR.

In a study done by Kandel *et al*<sup>49</sup> in Kathmandu, the MRSA was found to be 46.0% by disc diffusion method out of which 72.2% were *mecA* gene positive. In 2023, Khanal *et al*<sup>50</sup> reported a higher prevalence (46.6%) of MRSA based on the detection of *mecA* gene. Syangtan *et al*<sup>51</sup> reported 69.6% MRSA in clinical samples and 27.3% in environmental samples. Among these, 18.2% harbored pantone-valentine leucocidin gene. Last year Manadhar *et al*<sup>52</sup> reported the prevalence of MRSA as 60.0% at a tertiary care hospital in Kathmandu. Of them, 21.7% were *mecA* gene negative. A significantly greater prevalence of the *mecA* gene in the biofilm producing isolates (54.6%) than in the non-biofilm producing isolates (45.3%) was detected, and biofilm producing *S. aureus* isolates were mostly MDR. They have also claimed that they are the first to explore the associations between SCCmec types and biofilm formation among clinical isolates in Nepal. Ghimire *et al*<sup>53</sup> reported the MRSA prevalence of 28.9% and 3.8% were vancomycin resistant (VRSA). In their study they found *mecA* gene 50.6% of MRSA isolates whereas *vanA* gene was detected in 40.0% of VRSA cases. Bhatta *et al*<sup>54</sup> in western Nepal found a 34.7% of MRSA out of which *mecA* gene was positive in 56.8%. Raut *et al*<sup>55</sup> in Palpa reported MRSA prevalence of 43.6% and were MDR, However, none of them were VRSA.

Dhungel *et al*<sup>56</sup> reported a very high prevalence of MRSA (87.2%) among cardiac patients at a tertiary care heart center in Kathmandu and out of them 94.1% were positive for *mecA* gene. In an another study, Gaire *et al*<sup>57</sup> reported MRSA in 55.6% of isolates at Sukraraj Tropical and Infectious Disease Hospital in Kathmandu whereas 44.0% were MDR. Adhikari *et al*<sup>58</sup> reported a significantly low prevalence of MRSA (26.4%) in Kathmandu as detected by disc diffusion method. The major sources of MRSA was pus and MDR was common among MRSA. Of the MRSA, 53.3% were positive for *mecA* gene.

**MRSA in health care workers:** Pant and Rai<sup>59</sup> reported the MRSA prevalence of 9.5%, 3.1% and 1.6% among *S. aureus* isolates isolated from nose, hand and hospital environment, respectively at a tertiary care center in Kathmandu as done by disc diffusion method.

Shrestha *et al*<sup>60</sup> reported nasal carrier rate of 2.3% of MRSA among health care workers (HCW) by disc diffusion method (oxacillin and cefoxitin). In a study, Mukhiya *et al*<sup>61</sup> reported the overall prevalence of MRSA of 45.9% at a hospital in Kathmandu as detected by disc diffusion method. The prevalence of MRSA was higher among HCWs (50.0%) compared with hospital environment (40.7%). Sah *et al*<sup>62</sup> reported the nasal carrier rate of *S. aureus* in 20.4% among hospital personnel in Birgunj and of the *S. aureus* isolates, 45.5% were MRSA as detected by disc diffusion method. In an another study Khanal *et al*<sup>63</sup> reported the MRSA prevalence of 21.9% among the *S. aureus* isolates isolated from the nose of HCWs working at a tertiary care hospital in Bhairahawa. HCWs of both surgical wards and operating room accounted for 28.6% of MRSA carriers. Pant and Sharma<sup>64</sup> reported MRSA carrier rate of 58.0% among HCWs in their nose and hands in Kathmandu as detected by disc diffusion method. In their study, MRSA was higher among nasal isolates. They also found that only 14.0% of the HCWs had proper knowledge about MRSA and use of personal protective equipment, adherence to hand hygiene, treatment of MRSA carriers with mupirocin etc and only 8.0% of HCWs were following the infection control policies strictly. Khatri *et al*<sup>65</sup> from KMC Teaching Hospital, Kathmandu reported the MRSA prevalence (nasal carrier rate) of 41.3% among HCWs as detected by cefoxitin disc and minimum inhibitory concentration (MIC) of oxacillin. They found a higher prevalence of MRSA was found among clinical lab workers followed by nurses. In a study done by Jha *et al*<sup>66</sup> nasal carriage rate *S. aureus* of 5.0% among the HCWs of a Teaching Hospital in Kathmandu of which 40.0% were MRSA as detected by disc diffusion method.

Joshi *et al*<sup>67</sup> reported HCWs and patients carrying *S. aureus* at their nose in Kathmandu. Of them 21.5% were MRSA as detected by *mecA* gene. Nasal carriage rate was highest among nurses (13.6%) followed by ward patients (6.4%) and others. Fifteen MRSA isolates were resistant to high-level mupirocin (51.0% MICs >1024 µg/ml) and mupirocin resistant gene (*mupA* gene) was found in 14 isolates and *mupB* gene in 1 isolate. Giri *et al*<sup>68</sup> reported a 35.3% prevalence of MRSA colonizing the anterior nares of HCWs working at a Teaching Hospital in Kathmandu as detected by disc diffusion method. MRSA colonization was highest among doctors. Rijal *et al*<sup>69</sup> reported MRSA prevalence of 5.2% among *S. aureus* isolated from the nose of HCWs at a Teaching Hospital in Kathmandu. Among the MRSA, 83.3% were biofilm producer,

however, none of the isolates were resistant to vancomycin. In another study done by Rai *et al*<sup>70</sup> an overall prevalence of 45.3% of MRSA has been detected among HCWs working at a teaching hospital in Kathmandu by the detection of *mecA* gene. All MRSA were isolated from nose (48.9%). Interestingly, none (0/10) of the re-colonized carrier (after successful treatment with mupirocin) were MRSA. Adhikari *et al*<sup>71</sup> reported the MRSA prevalence of 35.5% as detected by cefoxitin disc diffusion method. By oxacillin broth microdilution method, 31.82% of the *S. aureus* isolates were found to be MRSA. However, *mecA* gene was present in only 29.1% of the isolates.

Shrestha *et al*<sup>72</sup> have also studied the knowledge regarding MRSA among nurses in the selected Hospital of Kathmandu by using self-administered structured questionnaire. Among the nurses included, majority of respondents (53.7%) demonstrated a high level of knowledge, while 19.5% had a moderate level and 26.8% showed a low level of knowledge indicating that over half of the participants were well-informed about MRSA.

***MRSA in dumpsite workers, school children and others:*** Manandhar *et al*<sup>73</sup> have reported a relatively low prevalence of nasal carrier rate of MRSA among dumpsite workers (7.5% in males and 5.0% in females) in Nepal. Joshi *et al*<sup>74</sup> have reported the MRSA nasal carrier rate of 5.2% among healthy school children in Kathmandu Valley as detected by disc diffusion method. Kapali *et al*<sup>75</sup> at a hospital in Kathmandu, found the nasal carrier rate of MRSA in 3.7% of people living with HIV compared with healthy cohort controls (5.0%). All of the MRSA isolates

from both groups had *mecA* gene (100.0%), however, there was no statistically significant difference in the presence of *PVL*-positive MRSA between the two groups. Robert *et al*<sup>76</sup> have reported MRSA in swine (kept in farm) (2.1%) and monkey (*Macaca mulatta*) (6.8%) population in Nepal by detecting the human clone *ST22 SCCmec IV* gene. In another study, they<sup>77</sup> reported the MRSA prevalence 17.5% in *S. aureus* isolated from Nepalese primates as detected by genomic analysis. Joshi *et al*<sup>78</sup> have also reported MRSA in dairy farms in Pokhara by cefoxitin disk diffusion method indicating presence of MRSA in farm animals. Sharma *et al*<sup>79</sup> reported 39.5% of MRSA in the door handles of selected hospitals in Pokhara, Nepal as detected by disc diffusion method. Rijal *et al*<sup>80</sup> reported the MRSA prevalence of 56.1% in healthy school children and 75.5% in patients attending a hospital in Pokhara as detected by disc diffusion method. The prevalence of MRSA was significantly higher in patients compared with healthy school children. Marasini *et al*<sup>81</sup> reported 33.3% prevalence of MRSA on “paper currency notes” in Pokhara by disc diffusion method.

**MRSA and VRSA in Nepal:** There are multiple reports of vancomycin susceptible MRSA isolates from Nepal.<sup>28,31,37,45,71</sup> In 2021, Maharjan *et al*<sup>46</sup> reported that among the 45 MRSA isolates, 11.1% were vancomycin resistant as tested by MIC using vancomycin strips (E-Test) and out of these five, two (40.0%) were VRSA as they were positive for *vanA* gene. Later, in 2023, Khanal *et al*<sup>50</sup> reported none of the MRSA isolates harbored vancomycin-resistant (*vanA* gene) while another study by Nepal *et al*<sup>82</sup> stated that

**Prevalence of *mecA* gene positive human and monkey MRSA in Nepal**

| n  | Authors                                                                 | Year | <i>mecA</i> gene +ve % | Source                                                                 |
|----|-------------------------------------------------------------------------|------|------------------------|------------------------------------------------------------------------|
| 1  | Bhatta <i>et al</i> <sup>54</sup>                                       | 2016 | 56.8                   | <i>BMC Infect Dis</i>                                                  |
| 2  | Joshi <i>et al</i> <sup>67</sup>                                        | 2017 | 21.5                   | <i>Asia Pacific J Trop Biomed</i>                                      |
| 3  | Adhikari <i>et al</i> <sup>71</sup>                                     | 2017 | 29.1                   | <i>Can J Infect Dis Med Microbiol</i>                                  |
| 4  | Kandel <i>et al</i> <sup>49</sup>                                       | 2020 | 72.2                   | <i>SAGE Microbiol Insights</i>                                         |
| 5  | Kapali <i>et al</i> <sup>75</sup>                                       | 2021 | 100.0                  | <i>Future Sci OA</i>                                                   |
| 6  | Gaire <i>et al</i> <sup>57</sup>                                        | 2021 | 53.3                   | <i>Diseases</i>                                                        |
| 7  | Dhungel <i>et al</i> <sup>56</sup>                                      | 2021 | 94.1                   | <i>Infect Dis (Auckl)</i>                                              |
| 8  | Khanal <i>et al</i> <sup>50</sup>                                       | 2023 | 46.6                   | <i>Nepal Med Coll J</i>                                                |
| 9  | Nepal <i>et al</i> <sup>82</sup>                                        | 2023 | 84.2                   | <i>Microbiol Insights</i>                                              |
| 10 | Ghimire <i>et al</i> <sup>53</sup>                                      | 2024 | 50.6                   | <i>J Nepal Health Res Counc</i>                                        |
| 11 | Rai <i>et al</i> <sup>70</sup>                                          | 2024 | 45.3                   | <i>Nepal Med Coll J</i>                                                |
| 12 | Manandhar <i>et al</i> <sup>52</sup>                                    | 2025 | 21.7                   | <i>BMC Infect Dis</i>                                                  |
| 13 | Roberts <i>et al</i> <sup>76</sup><br>(in <i>Macaca mulatta</i> monkey) | 2018 | 6.8                    | FEMS Microbiol Ecol<br>( <i>ST22 SCCmec IV</i> gene has been detected) |

47.5% were phenotypically confirmed MRSA out of which 84.2% had *mecA* gene. Of them, two isolates were found to possess the *vanB* gene. In a study done in Kathmandu by Ghimire *et al.*,<sup>53</sup> 3.8% (n=10) were VRSA but *vanA* gene was detected only in 4 (40.0%) of VRSA cases.

In conclusion, the MRSA first reported by Jevons<sup>4</sup> in England in 1961, has now spread all over the world with the pooled global prevalence of MRSA has been reported to be 14.7%.<sup>13</sup> In Nepal, MRSA was reported in 1990 by Rai *et al.*<sup>23</sup> in 1990. Since then, increasing reports have come to light from different parts

of country from clinical cases, healthcare workers as well as environment.<sup>24-82</sup> The rate of *mecA* gene positive MRSA in Nepal ranges from 21.5 to 100% and many of them are MDR strains. In addition, MRSA has also been reported from door handles,<sup>79</sup> farm animals,<sup>78</sup> bank currency notes<sup>81</sup> as well as monkeys<sup>76,77</sup> in Nepal. These findings urgently demand the implementation of effective antimicrobial stewardship and good infection control practices along with regular surveillance of MRSA and VRSA.

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