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Evaluating the effectiveness of pneumococcal vaccines against hospitalization and intensive care unit admissions in adults

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2 intensive care unit admission in adults

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22 **Abstract**

23 Objective: To evaluate the efficacy of pneumococcal vaccines concerning hospital or
24 intensive care unit (ICU) admissions due to pneumonia after vaccination.

25 Setting: Inpatient and ICUs at Hamad General Hospital.

26 Methods: The retrospective study included adults who were vaccinated between June
27 2012 and June 2013. Patient records were reviewed for hospital or ICU admissions due to
28 pneumonia two years before and after vaccination.

29 Main outcomes measures: The primary outcome was to compare the rates of hospital and
30 ICU admissions for pneumonia two years before and after vaccination.

31 The secondary outcome was to evaluate the efficacy of pneumococcal vaccines against
32 different comorbidities.

33 Key findings: One hundred sixty-one patients were included with a dominant age group
34 of 64–85 (52%) years old. Comorbidities reported were hypertension (HTN), diabetes
35 mellitus (DM), chronic obstructive pulmonary disease (COPD) and asthma. The rate of
36 hospital admission due to pneumonia was significantly reduced within two years after
37 vaccination, 71% to 39% ($p < 0.001$). There was a trend toward reduced ICU admission
38 (12.4% to 10.6), but the results did not achieve statistical significance ($p > 0.72$).

39 In diabetic, hypertensive and COPD/Asthma patients, there was a statistically significant
40 reduction in hospitalization. Although there was a reduction in ICU admission for both
41 commodities the results did not achieve statistical significance

42 Conclusion: Adults who received pneumococcal vaccines experienced reduced rates of
43 hospital versus ICU admissions due to pneumonia infection.

44

45 **INTRODUCTION**

46 Pneumococcal and influenza infection can cause significant morbidity and infection-
47 related mortality. In 2006, pneumonia and influenza together were ranked as the eighth
48 leading cause of death in the United States of America (USA) (1). In 2006, 55,477 people
49 died of pneumonia in the USA (2). Throughout the last decade direct and indirect costs
50 for pneumococcal and influenza infections have been estimated to be in millions (1).
51 Pneumonia has become a worldwide concern due to its high prevalence and impact on
52 health care systems. Yearly in USA, pneumonia infection accounts for 500,000 case of
53 respiratory tract infection (RTI), 50,000 cases of bacteremia, and 3,000 cases of
54 meningitis (2). There were no exact epidemiological studies for pneumonia in Qatar.
55 Pneumococcal vaccines recommended being administered in high-risk populations, such
56 as elderly (over 65 years of age) and younger adults with underlying health problems
57 such as chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM),
58 congestive heart failure (CHF), and sickle-cell anemia. Patients with diseases that impair
59 the immune system (such as acquired immune deficiency syndrome AIDS) and those
60 undergoing cancer therapy or organ transplantation, or patients with other chronic
61 illnesses are particularly vulnerable and therefore need to be vaccinated (3). Besides,
62 immunizing eligible patients with influenza and pneumococcal vaccines is considered an
63 inpatient quality healthcare standard. Eventually, vaccination can help in prevention and
64 diminish antibiotic resistance through its ability to reduce their use. Furthermore,
65 pneumococcal vaccination and influenza vaccine was found to have a cardioprotective
66 effect (4). Of note, the administration of the influenza vaccine showed an additive

67 protective impact regarding in-hospital mortality from pneumonia and cardiac failure
68 among elderly patients (5).

69

70 More than 90% of all pneumococcal infections can be prevented by a single
71 pneumococcal vaccine, which protects against 23 different types of streptococcus
72 pneumonia (5). Approximately 50% of these deaths could be avoided through the use of
73 the pneumococcal vaccine (6). Simonsen et al. suggested that patients over 18 years old
74 are the age group with more than 90% of the benefit for vaccination regarding death and
75 hospitalizations (7).

76 On the other hand, a meta-analysis of 22 randomized and non-randomized clinical studies
77 evaluating the efficacy of the pneumococcal polysaccharide vaccine showed that the
78 vaccine doesn't appear to be effective against pneumonia, even among the recommended
79 population (8).

80 A double-blind, randomized control, single-centre trial covering 84,496 patients
81 randomly assigned to receive either the 13-valent polysaccharide pneumococcal vaccine
82 or a placebo, with a four-year follow-up, showed a 45% reduction of vaccine-type
83 community-acquired pneumonia (CAP) ($p = 0.0006$), a 45% reduction in non-
84 invasive/non-bacteremia CAP ($p = 0.0067$), and a 75% reduction in invasive vaccine-type
85 pneumococcal disease. Additionally, the study emphasizes a favorable safety profile (1).

86 There is a scarcity of data about the pneumococcal vaccine effectiveness amongst the
87 Middle East and North Africa (MENA) region and particularly in Qatar. Hence, the
88 vaccine effectiveness in term of hospitalization and ICU admission reduction was

89 evaluated amongst a group of patients who received the pneumococcal vaccine during the
90 study period in a tertiary teaching hospital

91 **Aim of the study**

92 To evaluate the effectiveness of pneumococcal vaccines in reducing hospital and
93 intensive care unit admissions due to pneumonia in immunized adult patients within two
94 years of immunization compared with the cross-matched case group in age and
95 comorbidities.

96 **Method**

97 **Study design and setting.**

98 This retrospective study included all adult patients (18 years of age or older) who were
99 admitted to the medical ward for any medical reason, and received a pneumococcal
100 vaccine (Pneumococcal conjugate vaccine (PCV-13) and/or pneumococcal
101 polysaccharide vaccine (PPV-23)) upon their discharge from Hamad General Hospital,
102 Qatar, between June 2012 and June 2013. We excluded pregnant women, patients on
103 dialysis and patients who had organ transplants mainly kidney or liver on regular immune
104 suppressants. Hamad General Hospital is a 603-bed tertiary care center that covers all
105 specialties except for hematology, oncology, cardiology, and obstetrics. It has been
106 accredited by Joint Commission International (JCI) since 2006.

107 **Source of information and data collection.**

108 Data were collected from a quality project done in Hamad General Hospital in 2012 and
109 2013(9). The project aimed to estimate the rate of the hospital compliance with the
110 recommendations from national and international guidelines, such as the Center for
111 Disease Control and Prevention guidance (CDC). Followed by a retrospective chart

112 review for all hospital and ICU admissions two years before the vaccination year June
113 2012 to June 2013(June 2010 to June 2012) and two years after (June 2013to June
114 2015). Data were secured in a particular form that included patient demographics, clinical
115 characteristics, laboratory results, and outcomes. This study was approved by the Hamad
116 General Hospital research committee as well as the Hamad Medical Corporation
117 institutional review board (IRB),
118 Diagnosis of Pneumonia was considered according to Physician's notes, X-rays,
119 microbiological results. Patients who had an admitting diagnosis of pneumonia with chest
120 X-ray changes with or without microbiological results—were counted as a pneumonia-
121 related infection.

122 **Outcomes**

123 The primary outcome was an evaluation of the rate of hospital and ICUs admissions due
124 to pneumonia. The secondary outcome was an evaluation of the effectiveness of
125 pneumococcal vaccines amongst different comorbidities.

126 **Statistical analysis**

127 Data were analyzed descriptively using percentages, frequencies and means standard
128 deviations for interval variables. Chi-square tests were performed to identify significant
129 associations between pneumococcal vaccinations in medical ward and ICU hospital
130 admissions. All analysis was conducted using SPSS.PASW. Statistical software version
131 18.

132

133 **Results**

134 The study included 161 patients, of them 60% were male, and 52% were in the age group
 135 64-85 years old. Comorbidities included diabetes (57% of patients), hypertension (70%)
 136 and COPD or asthma (45%) as displayed in (Table 1). The rate of hospital admission due
 137 to pneumonia was significantly reduced within two years after vaccination, from 71% to
 138 39% ($p < 0.001$), as illustrated in (Fig. 1). There was a trend towards reduced ICU
 139 admissions, (12.4% to 10.6%) but the results did not achieve statistical significance (p
 140 >0.72).

141 For the secondary outcomes, diabetic and hypertensive patients who were vaccinated had
 142 a statistically significant reduction in hospital admission after vaccination. Hospital
 143 admission dropped from 70.7% to 37.0% ($p < 0.0001$) for patients with diabetes and from
 144 71.7% to 39.8% ($p < 0.0001$) for those with hypertension. However, there was no
 145 statistically significant reduction in ICU admission—14.1% to 12% ($p >0.824$) and
 146 12.4% to 13.3% ($p > 1.0$) for diabetes and hypertension, respectively (Fig. 2). In patients
 147 who had asthma or COPD, vaccination did show significant reduction in hospital but not
 148 in ICU admissions 75.0% to 36.1% ($p < 0.001$) and 11.1% to 8.3% ($p > 0.774$),
 149 respectively.

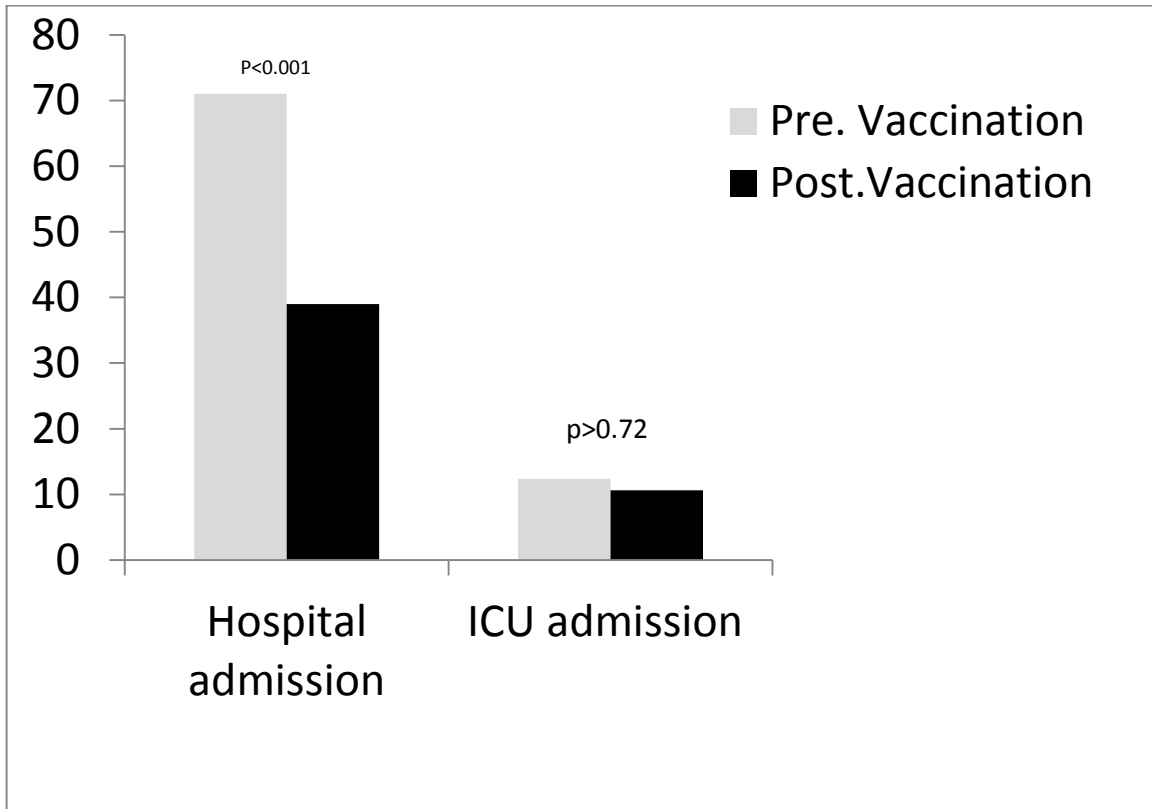
Table 1: Baseline Characteristics	
<i>Gender</i>	
Male	97 (60%)
Female	64 (40%)
<i>Age Group</i>	
Group 1 (18–40 yrs.)	16 (9.9%)
Group 2 (41–63 yrs.)	35.4 (22.3%)
Group 3 (64–85 yrs.)	84 (52.0%)
Group 4 (≥ 86 yrs.)	26 (15.8%)
<i>Comorbidities</i>	
Diabetes	(57.0%)
Hypertension	(70.0%)

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Asthma/COPD	(44.7%)
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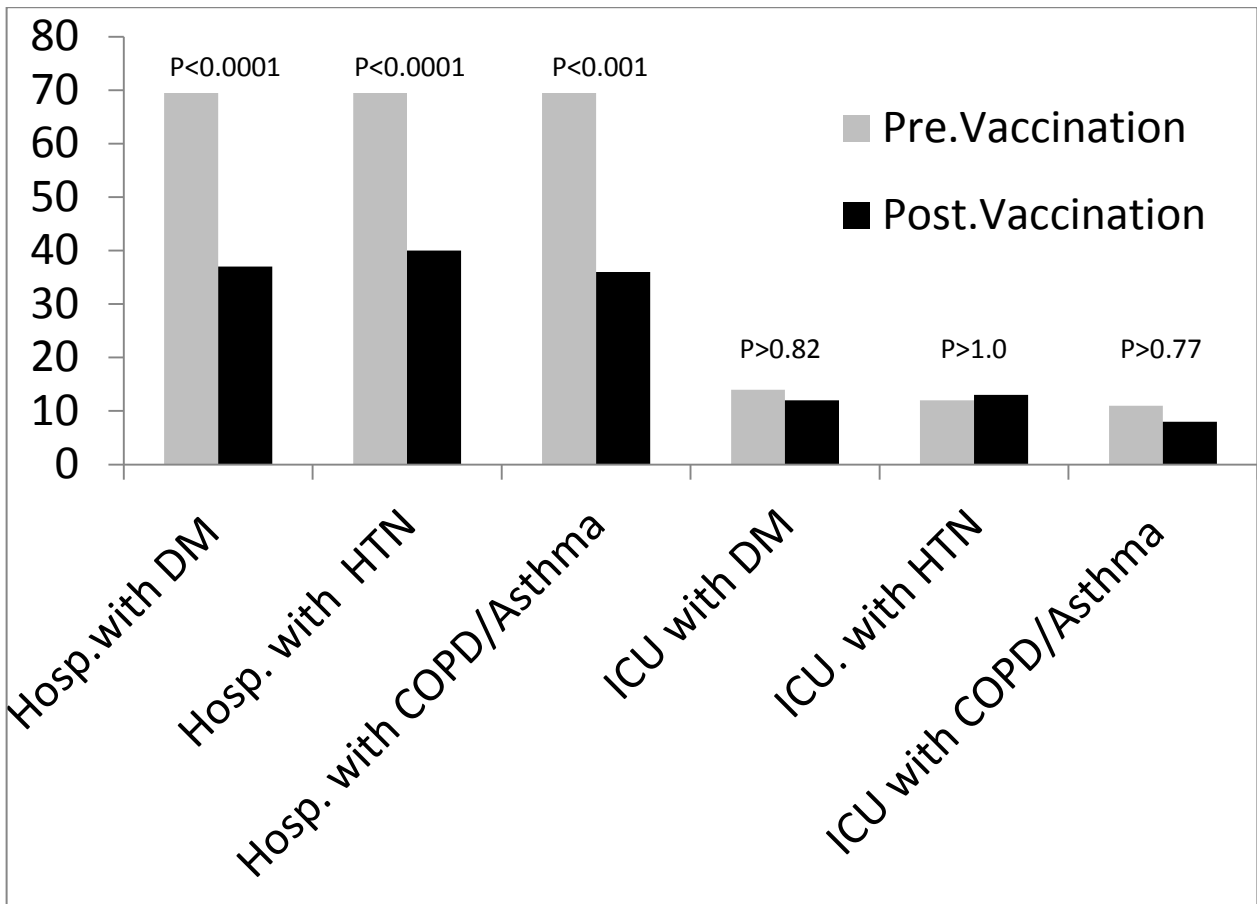
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155 Fig. 1, Percentage of hospital and ICU admissions due to pneumonia

156 pre and post vaccination

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160 Fig. 2, Sub-group analysis of hospital and ICU admissions pre and post vaccination due
161 to pneumonia according to patient's comorbidities (HTN, DM and COPD/Asthma)

162

163

164 Discussion

165 The results of this study show that pneumococcal vaccines reduced hospital admissions
166 among adults. It also shows some protection against hospital admissions for pneumonia
167 with specific comorbidities. Our findings are supported by the recommendation of the
168 scientific committee of the Infectious Disease Society of America (IDSA) in its

169 guidelines for the management of community-acquired pneumonia CAP in adults (10).In
170 which those groups with similar comorbidities are eligible for pneumococcal vaccination.
171 (10). Pilishvili et al. found that hospitalization notably declined in older adults (age >
172 years old) where the disease burden from pneumonia was substantial and in-hospital
173 mortality was estimated at up to 12% (11).

174 The current study appears to be the first to evaluate and differentiate the vaccine
175 effectiveness in regards to different hospital admissions (Hospital and ICU admissions).

176 Pneumococcal vaccines showed a decreasing trend in ICU admissions related to
177 pneumonia, but it was not statistically significant; however, this could be attributed to the
178 small sample size. These results were consistent with a meta-analysis of 22 trials that
179 included 101,507 participants, which found that vaccinations didn't prevent death,
180 pneumonia, or invasive pneumococcal infections. However, this meta-analysis did not
181 take into consideration the rate of hospitalization (8).

182 Ortqvist et al. conducted the first randomized control trial that evaluated the effectiveness
183 of PPV-23 in preventing pneumonia in the elderly. This was a multicenter study that
184 included 691 participants aged 50–85 years. Participants were randomized to receive
185 PPV-23 or a placebo after being hospitalized for CAP and were followed up within 2.5
186 years. In the vaccinated group, 19% developed pneumonia versus 16% in the placebo
187 group. The relative risk for the placebo group was 0.83 (95% CI 0.58–1.12, $p = 0.31$).
188 However, this study was underpowered, and the new recommendations came with the
189 administration of PCV followed by PPV, or vice versa according to age and
190 comorbidities (12,13).

191 Johnstone et al. followed up two thousand nine hundred fifty patients who received PPV
192 while being admitted with CAP, for five years after discharge. In this population-based
193 cohort study, Johnstone et al. did not find a significant reduction in either death or
194 hospitalization with PPV. However, the inclusion of some co-infected pneumonia
195 patients was considered as a study drawback 14).Despite being the first study to measure
196 the vaccines' efficacy on preventing ICU admission, the current study had several
197 limitations. Neither the mortality cases that were admitted to the ICU due to pneumonia,
198 nor the 28 days mortalities after ICU discharge were considered because the study was
199 examining the risk and the probability of decreasing admission. It was challenging to
200 include or consider cardiovascular patients in a subgroup analysis because those patients
201 will be admitted to the heart hospital, which is a different facility with its ICU. Including
202 patients vaccinated with pneumococcal and annual influenza vaccine is a significant
203 limitation of this study. However, this was considered as the data collection was during
204 the immunization season e. Differentiating and subgrouping the patients to further two
205 groups according to each pneumococcal vaccine was hard to attempt, as the data was
206 taken from a quality project that was done to ensure that eligible patients were
207 vaccinated. The new recommendations are that each patient will receive the two types of
208 vaccination but through different time intervals. Giving that our study proved that any of
209 the pneumococcal vaccines had a protective role in regards to hospital admission.

210

211 In the findings for asthma and COPD one of the highest-risk groups for pneumonia
212 infection and admissions, the vaccine showed an ability to protect and only reduce
213 hospital and ICU admissions. Several explanations could be behind these findings; one of

214 the most cited reasons is the failure of the vaccine to maintain antibody response. Musher
215 et al. studied participants who received PPV then PCV after six months (15), or vice-
216 versa. The patients' immunoglobulin G (IgG) was measured at baseline, four to eight
217 weeks, and six months after each vaccine. At six months, the IgG had returned to its
218 original baseline levels, questioning the beneficial effect of pneumococcal vaccines in
219 adults (15).

220 Conclusion

221 The pneumococcal vaccine is effective in reducing hospital admission amongst diabetic,
222 hypertensive and COPD/Asthma patients, however the clinical significance of
223 pneumococcal vaccines in decreasing hospital and ICU admissions as well as the age-
224 specific concomitant comorbidities that will highly benefit from the vaccine and the
225 timing of the booster doses must be determined in more extensive long-term clinical trials
226 in the future.

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294 **Figure legends list**

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296 and post vaccination

297 Fig. 2, Sub-group analysis of hospital and Intensive Care Unit admissions pre and post
298 vaccination due to pneumonia according to patient's comorbidities (HTN, DM and
299 COPD/Asthma)

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