Study of adverse events of A/H1N1 vaccine among health care staff in selected provinces of Afghanistan, 2010

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دراسة الأحداث الضائرة للقاح الإنفلونزا A/H1N1 بين العاملين في الرعاية الصحية في ولايات منتقاة من أفغانستان 2010

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الخلاصة: في نهاية شهر آذار/ مارس 2010 أجريت حملة تلقيح ضد الإنفلونزا A/H1N1 في أفغانستان باستخدام اللقاحات التي قدَّمتها أطراف مانحة؛ ولم يوضع موضع التنفيذ بعد التمنيع أي نظام للترصُّد لكشف الأحداث الضائرة التالية له. ويقدم الباحثون دراسة مستعرضة وصفية لمسح أجري في أربع ولايات في أفغانستان، استهدف تقييم معدل الأحداث الضائرة بين العاملين في الرعاية الصحية الذين تلقوا التمنيع باللقاح الوحيد التكافؤ المضاد للإنفلونزا A/H1N1، وذلك بعد مضي أربعة أسابيع على التلقيح. وقد استخدم الباحثون عينات تتناسب عشوائياً مع حجم الدراسة، وشملت 350 من العاملين (العمر الوسطي 36 عاماً، والمجال 16 إلى 65 عاماً)، وتم التحرّي باستخدام استبيان. وقد كانت أعلى المعدلات للأحداث الضائرة التي تم الإبلاغ عنها هو الألم في موضع الحقن (53٪)، والحمى في الأيام الثلاثة الأولى التي أعقبت التمنيع (40٪)، والآلام الجسدية (39٪)، والتعب (33٪)، وتورم موضع الحقن (29٪)، واحمرار موضع الحقن (28٪). وقد عانت النساء أكثر مما عانى الرجال من التفاعلات الضائرة واختلفت المعدلات بين ولاية وأخرى، مُتَراوِحةً بين 79٪ في بلخ و23٪ في كابل.

ABSTRACT At the end of March 2010 an A/H1N1 vaccination campaign was conducted in Afghanistan using donated vaccines. However, no surveillance system for detection of adverse events following immunization was in place. We report a cross-sectional, descriptive survey in 4 provinces of Afghanistan to assess the rate of adverse events among health care staff immunized with A/H1N1 monovalent vaccine 4 weeks after vaccination. Using random sampling proportionate to size, 350 staff (mean age 36 years, range 16–65 years) were surveyed using a questionnaire. The highest self-reported rates of adverse events were pain at the injection site (53%), fever in the first 3 days after immunization (40%), body pain (39%), tiredness (33%), swelling at the injection site (29%) and redness at the injection site (28%). More females than males suffered adverse reactions and the rates varied across different provinces, ranging from 79% in Balkh to 23% in Kabul.

Étude des manifestations indésirables suite à la vaccination contre la grippe A (H1N1) chez les agents de santé dans des provinces afghanes sélectionnées sur l'année 2010

RÉSUMÉ Fin mars 2010, une campagne de vaccination contre la grippe A (H1N1) a été menée en Afghanistan avec des vaccins faisant l'objet de dons. Toutefois, aucun système de surveillance pour détecter les manifestations postvaccinales indésirables n'était en place. Nous transmettons les résultats d'une enquête descriptive transversale, menée dans quatre provinces de l'Afghanistan pour évaluer le taux de manifestations postvaccinales indésirables chez les agents de santé vaccinés avec le vaccin monovalent contre la grippe A (H1N1) quatre semaines après l'injection. Sélectionnés par échantillonnage aléatoire proportionnel, 350 agents de santé (âge moyen: 36 ans, fourchettes : 16–65 ans) ont participé à l'enquête en répondant à un questionnaire. Les manifestations postvaccinales indésirables les plus fréquemment déclarées étaient une douleur au niveau du site d'injection (53 %), de la fièvre dans les trois premiers jours suivant la vaccination (40 %), des courbatures (39 %), de la fatigue (33 %), un gonflement (29 %) ou une rougeur (28 %) au niveau du site d'injection . Les femmes étaient plus nombreuses que les hommes à être affectées par des réactions indésirables et les taux de réaction variaient entre les provinces, allant de 79 % dans la province de Balkh à 23 % dans la province de Kaboul.

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Introduction

Emergence of the A/H1N1/2009 virus in early 2009 was the trigger for the first pandemic influenza this century [1]. The virus spread to several countries within weeks, which reduced the possibility of rapid containment to zero, and the World Health Organization (WHO) declared pandemic influenza on 11 June 2009 [2]. By the time the virus was detected it was widespread in Mexico, parts of the United States and Canada, hence the rapid containment of the disease was practically impossible, and other recommendations of the International Health Regulations, e.g. pharmaceutical and not pharmaceutical interventions, were implemented. On the principle of access to health and treatment, after declaration of phase 5, WHO started deploying 3 million doses of the antiviral drug osletamivir to Mexico and to 71 pre-identified low-income countries, of which 50 000 doses of the medicine reached Afghanistan by October 2009. Influenza A/H1N1 monovalent vaccine was licensed in September 2009 and was on the market by the end October 2009 [3,4]. Use of this vaccine was considered to be safe by producers, the Centers for Disease Control and WHO [5–9]. A total of 78 million doses of pandemic influenza vaccine were deployed to 77 countries in 2009 and 2010.

In February 2010 Afghanistan received 0.5 million doses of GlaxoSmithKline pandemic influenza vaccine to protect the health workforce, pregnant women, young children and people with chronic illnesses. The Ministry of Public Health in Afghanistan decided to vaccinate health care staff first and planned to receive more vaccine for other high-risk groups later. Influenza vaccination was not part of the routine regime of vaccination in the country and therefore no surveillance system for detection of adverse events following immunization (AEFI) with influenza vaccine was in place. Also as the vaccines reached Afghanistan at the peak of pandemic influenza, the vaccination campaign was conducted immediately to ensure the integrity of the health system in Afghanistan and prevent a collapse in the system. This paper reports a survey to assess the rate of self-reported AEFI among a sample of health care staff immunized with A/H1N1 monovalent vaccine in 4 provinces of Afghanistan in 2010.

Methods

Study design

This was a descriptive, cross-sectional study with a simple random sampling proportionate to size method. Afghanistan received the donation of vaccines from WHO in February 2010 and the vaccination campaign was conducted at the end of March 2010. This study was conducted at the end of April 2010, just over 4 weeks after administration of the vaccines.

Study setting and sample

The study was conducted in the 4 major provinces of Kabul, Nangarhar, Balkh and Herat. Health facilities in the selected provinces were the sampling frame and the subjects were health care workers who received H1N1 vaccination. Health care facilities were randomly selected from the list of health facilities that received the vaccine. Study candidates were also selected randomly from the list of the health care workers receiving vaccination in the respective health facilities. A total of 27 100 people received A/H1N1 monovalent vaccine in these 4 provinces of Afghanistan. *OpenEpi* was used to draw a sample of 417 from the pool of subjects.

Data collection

A questionnaire was developed, field tested and applied to all study candidates by a team of 11 qualified trained surveyors who conducted the interviews and filled the questionnaires. Oral consent from participants was obtained prior to interview. Reports of local AEFI were all subjective and based on the respondents' own reports. Reports of systemic AEFI were verified where possible by medical doctors and were registered.

Analysis

The data were entered to *Epi Info* database and analysed using *Epi Info* and Microsoft. *Excel* statistical packages. The rates of adverse reactions or adverse events were compared with the manufacturer's reported rate of adverse events following immunization with the influenza monovalent vaccine [10]. The manufacturer categorized the AEFI as: common (> 1/100 but < 1/10 people), uncommon (> 1 /1000 but < 1/100), rare (1/10 000 but < 1/ 1000) and very rare (< 1/10 000).

Results

Background characteristics

After excluding forms with inaccurate or missing data 360 of the selected candidates were included in the study: 91 (25%) females and 279 (75%) males; 86% were married. The mean age was 36 years, range 16–65 years. There were 137 in Kabul (103 males/34 females), 87 in Nangarhar (64 males/14 females), 66 in Balkh (48 males/18 females) and 80 in Herat (55 males/25 females). The distribution by educational level showed 44 (12%) staff with no education (i.e. ancillary staff), 23 (6%) primacy education, 13 (4%) secondary education, 39 (11%) high school graduates, 142 (39%) paramedical (12–15 years of education) and 100 (28%) university graduates.

Adverse events reported

Table 1 summarizes the rate of each adverse event. Pain at the site of injection

Table 1 Rates of adverse events following immunization of a sample of health staff in Afghanistan with A/H1N1 vaccine (*n* = 360)

Adverse event	Females (*n* = 91)		Males (*n* = 270)		Both sexes (*n* = 361)	
	No.	%	No.	%	No.	%
Pain at injection site	56	62.2	136	50.4	192	53.2
Body pain	44	48.9	96	35.6	140	38.9
Fever	44	48.9	100	37.0	144	40.0
Tiredness	33	36.7	87	32.2	120	33.3
Swelling at injection site	33	36.7	71	26.3	104	28.9
Hardness at injection site	29	32.2	57	21.7	86	23.9
Redness at injection site	27	30.0	72	26.7	99	27.5
Muscle pain	27	30.0	67	24.8	94	26.1
Chills	24	26.7	24	8.9	48	13.3
Headache	23	25.4	52	19.3	75	20.8
Muscle weakness	14	15.6	42	15.6	56	15.6
Shivering	12	13.3	15	5.6	27	7.5
Sweating	10	11.0	20	7.4	30	8.3
Fainting	9	10.0	24	8.9	33	9.2
Coryza	9	10.0	17	6.3	26	7.2
Hypotension	9	10.0	15	6.5	24	6.7
Numbness	6	6.7	12	4.4	18	5.0
Tingling	6	6.7	9	3.3	15	4.2
Insomnia	5	5.6	17	6.3	22	6.1
Tinnitus	5	5.6	9	3.3	14	3.9
Neuralgia	4	4.4	6	2.2	10	2.8
Generalized rash	4	4.4	4	1.5	8	2.2
Blurred vision	2	2.2	8	3.0	10	2.8
Hypertension	2	2.2	1	0.4	3	0.8
Bruising	2	2.2	1	0.4	3	0.8
Convulsion	1	0.0	2	0.7	3	0.8
Bleeding	1	0.0	1	0.4	2	0.6
Vasculitis	0	0.0	3	1.1	3	0.8

was the most common AEFI, reported by 53% of study participants. Other local reactions—swelling, redness and hardness at the injection site—were reported by 29%, 28% and 24% of respondents respectively. Some of the study participants (13%) experienced all the classic signs of local inflammation (heat, redness, swelling and pain).

The second most common AEFI was a systemic one, fever in the first 3 days after immunization, reported by 40% of respondents. Some of the respondents (9%) had all the signs of local inflammation plus fever and 5 (1%) reported all the injection site effects together with fever, body pain and shivering. Overall, 10% of the study participants reported influenza-like illness in the first 7 days after the influenza vaccination.

Body pain was the third most common complain, experienced by 39% of all those who received vaccine: 49% among females versus 36% among males. Other common complaints reported by respondents were: tiredness (33%), muscle pain (26%), headache (21%), muscle weakness (16%), chills (13%) and fainting (9%). Blurred vision, neuritis, bleeding, vasculitis and convulsions were rarely reported (0.3%, 0.3%, 0.6%, 0.8% and 0.8% respectively).

No infections at the site of injection, purulent discharge from the site of injection, anaphylactic shock or deaths were recorded after influenza immunization.

Adverse events reported by demographic characteristics

Feelings of pain at the injection site were experienced by more females (62%) than male respondents (50%). Fever was also more common among females

(54%) than males (37%). The rate of fever was 63% in Nangarhar, 56% in Herat, 49% in Balkh and 16% in Kabul. Pain at the injection site differed across residents of different provinces, ranging from 79% in Balkh to 23% in Kabul. The highest rate of pain among females was reported in Nangarhar province (93%), followed by Herat (84%), Balkh (72%) and Kabul (26%). Experience of AEFI also varied by educational level. Pain was reported more in those with only had primary education (83%), followed by university graduates (58%), high-school graduates (55%), no education (ancillary staff) (54%), paramedics (46%) and secondary education (39%).

Table 2 Comparison of the rates of adverse events in the current study in Afghanistan with data from the United States of America (USA) and Canada prior to the licensing of the A/H1N1 vaccine [5]

Adverse event	Rate of adverse event (%)		
	USA	Canada	Afghanistan (current study)
Pain	24	21	53
Fever	11	1	40
Fatigue	17	10	33
Redness	11	14	28
Swelling	10	6	29
Myalgia	13	11	26
Headache	28	10	21
Chills	5	3	13

Discussion

The study showed that the highest rate of AEFI was a local one—pain at the injection site—in 53% of participants. A systemic AEFI—fever—was reported by 40%. All the classic signs of local inflammation (heat, redness, swelling and pain) were reported by 13% of subjects. The findings of this study agree with a study conducted in Australia, in which the highest rate of adverse events were systemic (53.8%) and injection site events (56.3%) [11]. However, comparing the results of this study with similar studies conducted in the United States of America and Canada prior to the licensing of the A/H1N1 vaccine [5] (Table 2) show much higher rates of pain, redness and swelling at the injection site in our study and for all adverse events in this study except for headache. The findings were also not replicated in another study conducted in Canada in 2010 [12] and a multi-centre double-blind randomized trail conducted in China in 2009 in which the authors reported a local reaction of 5.3% and pain of 4.6% among a sample size of over 11400 individuals who received the first dose of the influenza vaccine [13]. However, a study in Canada reported that the incidence of AEFI was higher in those who received higher doses of the AH1N1 vaccine compared with those who received lower doses of the vaccine and this may be one of the reasons for a higher number of adverse effects in Afghanistan.

There are many factors that can contribute to higher rates of adverse effects following immunization: a higher dose than recommended may be administered, (e.g. > 15 μg); poor training of injectors may increase the risk of AEFI (e.g. shallow or deep injections may cause pain, redness and swelling of the injection site); and knowledge of participants about adverse events may lead to bias in answering. Among many difficulties that Afghanistan faced in this the first ever influenza vaccination campaign in the country were limited trained vaccinators, limited capacity for the logistic of vaccines which were not included in the routine immunization schedule, willingness of the vaccine recipients and attitudes of people toward the vaccine and vaccine safety.

This study had some limitations which should be noted. A cross-sectional study was conducted, while a prospective, cohort study would have been better. The results were a snapshot which was taken 4 weeks after vaccination. No objective measures were included in the study; all responses were based on the participants' self-reports and we could not clinically verify their responses because it was 4 weeks after the administration of the vaccine. As most of the reactions were mild and the study population was health care workers they were either self-treated or treated by colleagues without proper registration of the adverse event. No AEFI surveillance system for influenza vaccination was available in Afghanistan to compare our data with. The study was conducted only 4 weeks after implementation of the influenza vaccination campaign and therefore no delayed reactions/adverse effects were recorded.

Nevertheless, this was the first time that a major influenza vaccination campaign was conducted at the country level and it provides useful baseline data for future research. Implementation of an H1N1 vaccination campaign needs in-depth planning, logistics and training to reduce associated adverse effects and ensure injection safety. A proper AEFI surveillance system should be implemented to capture all events associated with the immunization.

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