

Storage of vaccines in different health centers and pharmacies at Karachi, Pakistan: The handling errors

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Abstract: The fundamental human desire is prevention from the infectious disease. Vaccine is the basic element to fulfill this human craving. The proper handling of vaccine can minimize the degradation. The main aim of this study is to find out the knowledge of respondents and storage condition and handling of marketed vaccines in different private clinics, hospitals and community pharmacies in Karachi, Pakistan. The present study revealed that ~77% have been allowed to visit their vaccine storage compartment. The cumulative knowledge of respondents regarding recommended temperature, shake test, thermal, freezing and photo degradation were 49.34%, 24.01%, 95.78%, 54.35% and 47.23% respectively. The major mishandling like the medicines, food and drinks and even laboratory specimen have been noticed 76.3%, 61.62% and 5.35% respectively. Moreover, water filled bottles on upper, lower and door shelves and ice packs or ice trays 3.43% and 14.18%, respectively, have been found in refrigerators and freezers, respectively. No expired vaccines have been found. The major consequence, in the study has been found to be mishandling by the absence of non-professional personnel. Either doctors or pharmacist (health associated professionals) as respondents were nearly all aware about the consequences of the mishandling of vaccines and have the knowledge about the recommended temperature, thermal, photo degradation, and freezing hazards of vaccines. The world-renowned immunization authorities have strongly recommended national/local immunization programs. On the basis of the present study, it is recommended to train the staff and prepare a national guideline for the storage and handling of vaccines, and forcefully implements the law to adopt the particular guideline.

Keywords: Vaccines, storage, awareness, healthcare centers, pharmacies

INTRODUCTION

The curing and aversion of sickness is additionally a testing condition for medicinal professionals. Microbes are found everywhere in atmosphere and its incursion may cause illness. Individuals resistance to microorganisms or have antibodies against particular microbes had fewer chances of fastidious infections (Arsalan *et al.*, 2014a; 2015). Vaccine plays a major role not only to provide a shield but aids in treatment (Favre and Viret, 2006; Faryal *et al.*, 2013). When vaccines are administered in body, this act as antigens and are produce antibodies as a defensive tool in the human beings (Daniell *et al.*, 2001). Vaccines, the biological products, act as safeguard are unstable and have been found to degrade, if not stored according to their recommended temperature and protected from light (Galazka *et al.*, 1998). Inappropriate storage and errors in handling can increase the cost of vaccine by revaccination. This may enhance the cost by repeated doses and diminish the patients' faith on vaccination. The administration of degraded vaccine may impair the immunity (Smith *et al.*, 2010). In 1993, around 41.5% polio multi dose vials have been desecrated in rural areas of Egypt (Setia *et al.*,

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2002). For the welfare of population, mishandled vaccine should not be administered.

Antibodies formed by vaccines have aided in the protection of different infections, not only infants but also in adults and even in pregnancy for many years (Yu *et al.*, 1999; Christenson *et al.*, 2001; Munoz *et al.*, 2005). The recommended temperatures are refrigerator storage temperatures between 35°F to 46°F (2°C to 8°C) and freezer temperature between -58° to +5°F (-50°C to -15°C). Toxoids, polysaccharides, protein based sub-units, conjugated polysaccharides are also known as inactivated vaccines. Inactivated vaccines are usually stored at refrigerator temperature. Live-attenuated vaccines should be stored at freezing temperature. DTaP vaccine, DT vaccine, Tdap vaccine, Td vaccine, hepatitis A vaccine, hepatitis B vaccine, HPV vaccine, Hib vaccine, influenza vaccine, meningococcal vaccine, pneumococcal vaccine, polio vaccine, rotavirus vaccine, DtaP-HepB-IPV (Pedarix), DtaP-IPV (Kinrix), DtaP-IPV/Hib (Pentacel), HepA-HepB (Twinrix), Hib-HepB (Comvax) should be stored in refrigerator. MMRV, vericella and zoster vaccines should be kept in freezer while MMR vaccines can be kept both in refrigerator and in freezer. All diluents should be kept at room temperature and protected from

light. Specific diluents of particular vaccine should be used for reconstitution (CDC, 2011). After reconstitution, the stability of vaccine was: varicella ≤ 30 mins (and protect from light); shingles ≤ 30 mins (and protect from light); MMR/varicella ≤ 30 mins (and protect from light); Yellow fever ≤ 1 hour; MMR ≤ 8 hours; single-dose vials (MPSV) vial ≤ 30 mins; DTaP/Hib ≤ 30 mins (DOH, OK). The recommended storage temperature of some vaccines is shown in Table 1.

Monovalent tetanus and diphtheria vaccinating agents are deteriorated at freezing temperature but possess stability against warmer temperatures as compared to pertussis and polio vaccines. Oral polio vaccine can be kept at freezing temperature, but repeated freeze thaw cycles should be avoided. BCG, MMR and oral polio vaccine (OPV) vaccines are unsteady at room temperature. Vaccines like DTP, MMR, OPV and meningococcal vaccines, influenza vaccine, Rotavirus vaccine, shingles can deteriorate from sunlight and fluorescent light (Page *et al.*, 2008).

The required temperature for the storage of vaccines is not found in the doors, top shelf, and floor of the refrigerator and/or freezer compartment. Moreover, daily fruit, and vegetable drawers are also not suitable for the storage of vaccines. It should be better that foods and beverages should not be stored in a vaccine storage unit. Frozen coolant packs can be stored in the freezer door. Refrigerated vaccines should not be stored near by the air vent, for the maintenance of temperature throughout the compartment, water filled bottles should be placed near by air vent, door and upper and lower compartment of refrigerator to reduce the risk of vaccines becoming too cold and only store vaccine that is not sensitive to the coldest temperatures (e.g., MMR). Defrost storage units are preferred for storage of vaccines (Jeremijenko *et al.*, 1996).

It has been an essential step to write the date and time on the vial of multiple dose vaccine. The same condition is also implied if single dose vials is not administered immediately after reconstitution. Usually single dose vials do not contain bacteriostatic agents and are used only for single time. Before reconstitution with diluents, all varicella-containing vaccines can be stored at refrigerator temperature for up to 72 hours continuously (Weber *et al.*, 1996). For any reason, filling of syringes in advance has been highly discouraged by CDC, because of the risk associated with the administration of vaccines. However, CDC has been recommended the use of manufacturer-supplied prefilled syringes for large immunization events and storage. The storage of vaccines at inappropriate temperature may deteriorate or reduce the potency of vaccines and can be increased the risk of reoccurrences of diseases which are prevented by vaccines. Such vaccines are not suitable to achieve the desired immunity after vaccination. Moreover, there is need of revaccination which may be burden on the pocket of the consumers

(CDC, 2011). A study regarding the temperature monitoring of vaccines in different health-care centers and pharmacies has been found that very low number of vaccines containing refrigerators and freezers have recommended temperature 35°F to 46°F (2°C to 8°C) and -58°F to +5°F (-50°C to -15°C) respectively (Arsalan *et al.* 2014b).

Visual inspection of vaccines has been an unreliable method of assuring that vaccine was stored under inappropriate conditions. Back-up generators should be facilitated for storing large vaccine inventories with continuous run of 72 hours. Inventory policy should be strictly abided as per rules and regulations to control the consumption of vaccines before expiry. Professional education of vaccine coordinator plays an important role to minimize the chances related to errors and/or storage (CDC, 2012). Mostly inactivated vaccines like DPT vaccine, hepatitis B vaccine, DPT-IPV vaccine and tetanus toxoid should be refrigerated and damaged by freezing and loss in the efficacy cannot be restored (WHO, 1980; Klotz *et al.*, 1986; Dimayuga *et al.*, 1995; Dietz *et al.*, 1997). The refrigerated vaccines should be checked by shaken test. In the era of late 1980s, shake test of vaccine has been developed. It has been used to determine the deterioration of absorbed vaccines. The bond between antigen and adsorbent has been broken due to freezing, leads to the formation of agglomeration of adsorbent. By repeated freezing and thaw cycles, the size and weight of agglomerate has been increased and settled down at the bottom of the packaging container (WHO, 2002; Milstien *et al.*, 2006). The most appropriate method is the shake test while visually observation of agglomerate under phase contrast microscope has been more clarified and identified cyro damage in vaccines. Precipitates with amorphous, crystalline, solid and needle like structure has been formed by freezing while vaccines stored at optimal temperature range (2-8°C) has shown fine-grain structure. It has been confirmed by scanning electron microscopy and X-ray analysis (Kartoglu *et al.*, 2010).

MATERIALS AND METHODS

The main aim of the study is to find out the prevalence of storage condition and temperature of marketed vaccines in different private clinics, hospitals, and community pharmacies in Karachi, Pakistan. Our study has been conducted from November 2012 to July 2013. During present study, we had visited 803 different clinics, centers, and pharmacies and found refrigerator and/or freezers in only 491 clinics, centers, and pharmacies. In these 491, 107 private clinics, 9 governmental healthcare centers, 56 hospital and 319 community pharmacies were selected randomly because they kept vaccines.

Furthermore, the type of refrigerator and/or freezer unit has been noted and temperature- monitoring thermometer and temperature records were also recorded. The location

Table 1: Recommended temperature of common vaccines

Refrigerator 35°F to 46°F (2°C to 8°C)	Freezer -58° to 5°F (-50° to -15°C)
Hepatitis vaccines	MMR vaccines (also be refrigerated)*
Pneumococcal vaccines	MMRV vaccines
Influenza vaccines	Varicella vaccines
Meningococcal vaccines	Zoster vaccines
Polio vaccines	
Rotavirus vaccines	
Diphtheria, Tetanus, Pertussis vaccines	

*MMR vaccines can be store in refrigerator and freezer.

Table 2: Knowledge of respondents and observation of storage and handling of vaccines

Observations	Private Clinics	Governmental Health Care Centers	Hospital Pharmacy	Community Pharmacy	Cumulative
Response Rate (Allow)	86/107 (80.37%)	8/9 (88.89%)	41/56 (73.21%)	244/319 (76.49%)	379/491 (77.19%)
Recommended Temperature Knowledge	73/86 (84.88%)	7/8 (87.5%)	39/41 (95.12%)	68/244 (27.86%)	187/379 (49.34%)
Thermal–Degradation Knowledge	86/86 (100%)	8/8 (100%)	41/41 (100%)	228/244 (93.44%)	363/379 (95.78%)
Freeze–Degradation Knowledge	81/86 (94.18%)	8/8 (100%)	39/41 (95.12%)	78/244 (31.96%)	206/379 (54.35%)
Photo–Degradation Knowledge	84/86 (97.67%)	8/8 (100%)	40/41 (97.56%)	47/244 (19.26%)	179/379 (47.23%)
Shake Test Knowledge	43/86 (50%)	6/8 (75%)	29/41 (70.73%)	13/244 (5.33%)	91/379 (24.01%)
Refrigerator Follow Recommended Temperature	65/86 (75.58%)	7/8 (87.5%)	36/41 (87.8%)	119/244 (48.77%)	227/ 379 (59.89%)
Freezer Follow Recommended Temperature	10/24 (52.63%)	5/8 (62.5%)	16/23 (69.57%)	48/220 (21.82%)	79/275 (28.73%)
Medication & Vaccine	14/110 (12.79%)	0/16 (0%)	51/64 (79.68%)	434/464 (93.53%)	499/654 (76.3%)
Foods & Drinks	17/110 (15.45%)	6/16 (37.5%)	36/64 (56.25%)	344/464 (74.13%)	403/654 (61.62%)
Laboratory Specimens	10/110 (9.09%)	2/16 (12.5%)	21/64 (32.81%)	0/464 (0%)	33/654 (5.05%)
Only For Vaccines	6/110 (5.45%)	16/16 (100%)	7/64 (10.93%)	6/464 (1.29%)	35/654 (5.35%)
Water Filled Bottles in Upper, Lower & Door Shelves	2/86 (1.16%)	5/8 (62.5%)	6/41 (14.63%)	0/244 (0%)	13/379 (3.43%)
Upper, Lower & Door Shelves (Vaccine Storage)	79/110 (71.81%)	2/16 (12.5%)	43/64 (67.18%)	451/464 (97.19%)	575/654 (87.92%)
Thermometer in Refrigerator/Freezer	2/110 (1.81%)	14/16 (87.5%)	6/64 (9.38%)	0/464 (0%)	22/654 (3.36%)
Inventory Policy (FEFO)	86/86 (100%)	8/8 (100%)	41/41 (100%)	244/244 (100%)	379/379 (100%)
Expired Vaccines	0/110 (0%)	0/16 (0%)	0/64 (0%)	0/464 (0%)	0/654 (0%)
Refrigerator/Freezer Life (more than 10 years)	20/110 (18.18%)	1/16 (6.25%)	5/64 (7.81%)	171/464 (36.85%)	197/654 (30.12%)
Lose Detectable Seal	14/110 (11.81%)	0/16 (0%)	3/64 (4.68%)	117/464 (25.22%)	134/654 (20.49%)
Ice Trays, Ice Packs	7/24 (29.17%)	8/8 (100%)	14/23 (60.87%)	10/220 (4.55%)	39/275 (14.18%)
Freezer Temperature Vaccine in Refrigerator	7/86 (8.14%)	1/8 (12.5%)	4/41 (9.75%)	20/244 (8.19%)	32/379 (8.44%)
Refrigerator Temperature Vaccine in Freezer	1/24 (4.17%)	0/8 (0%)	5/23 (21.74%)	11/220 (5%)	17/275 (6.18%)
Power Substitution for Vaccine Storage Compartments	1/86 (1.16%)	6/8 (75%)	37/41 (90.24%)	3/244 (1.22%)	47/379 (12.4%)
Opened Vial without Date	17/110 (15.45%)	0/16 (0%)	13/64 (20.31%)	0/464 (0%)	30/654 (4.59%)
Health Associated Professional Availability	86/86 (100%)	8/8 (100%)	38/41 (92.68%)	49/244 (20.08%)	181/379 (47.76%)

of vaccines in refrigerator, and in freezer, and the presence of expired vaccines has been an essential part of this study. Other information collected included respondents knowledge about vaccine storage and handling, presence of thermometer, presence of ice packs or ice trays, staff's professional education, shake test knowledge, inventory policies (first expire first out), storage compartment condition, power substitution in case of electricity failure, management of problems, storage of material other than vaccines (food, laboratory specimens, and medications).

RESULTS

As it has been found, cumulative response rate was 77.19%, greater part of the respondents were apprehensive about offense due to absence or lacking of implementation of rules in their clinics and pharmacies. Out of 491, cumulative 379 had obliged and grant us consent to visit their vaccine storage refrigerator and/or freezer, in which 86 were private clinics, 8 governmental healthcare centers, 41 hospital pharmacies and 244 community pharmacies, selected randomly. The prime

object of the study was to know the storage and handling of vaccines in clinics, pharmacies, and governmental healthcare centers. The study included information about respondents knowledge about vaccine storage and handling, presence of thermometer, presence of ice packs or ice trays, staff professional education, shake test knowledge, inventory policies (first expire first out), storage compartment condition, power substitution in case of electricity failure, management of problems, storage other than vaccines (foods, laboratory specimens, and medications). The location of vaccines in refrigerator, and in freezer at their respective suggested temperature, and the presence of expired vaccines and the professional education. The result has been summarized in Table 2 and graphically demonstrated in Fig.1.

DISCUSSION

Vaccines are the tool not only for the eradication of infectious disease, but also for its prevention (Gershon, 2001). Vaccine quality is the shared responsibility of all parties, from manufacturing until administration. Vaccines are perceptive biological products and degraded with the span of time. They have a specific shelf-life. Due to change in recommended temperature, if the vaccine cannot be stored properly; it may be degraded faster before its shelf-life. In developing countries, a number of factors have been involved by which vaccines may not be stored as recommended like non implementation of rules; lack of knowledge; guidelines; training; power broke down; economic crisis (CDC, 2012).

It is an embarrassing condition that only 49.34% respondents had knowledge of recommended storage temperature of vaccines, while positive sign $\geq 85\%$ respondents had remembered in private clinics, governmental health-care centers, and hospital pharmacy. The poor knowledge related to cold chain has also been found in Niassa, Mozambique (Mavimbe and BJune, 2007). According to a WHO report, it has been known that not only heat but also freezing and light also influence the potency of vaccines (Galazka *et al.*, 1998). It has been found cumulative 95.78% had known about the thermal-degradation, while only 54.35% were familiar about the destruction of some vaccines by freezing. It is an important point that $\geq 95\%$ or even 100% respondents in governmental health-care centers, private clinics and hospital pharmacy had known. Similarly, this 47.23% had information about the photo-degradation, the result of respondents of private clinic, and governmental health-care centers and hospital pharmacy were about same result regarding the knowledge of freezing recommended temperatures. Marlovits *et al.* (2000) have observed that the degraded vaccines induced systemic adverse reactions were rare while local reactions were of clinical significance (Marlovits *et al.*, 2000). The loss of potency of vaccines cannot be observed by naked eye, whereas,

some vaccines had shown clumping in the solution when the vial has been shaken. By the storage of vaccine in freezers, crystals were formed, e.g. shaking of DPT vaccine, crystals has been observed, it has been found that overall 24.01% knew about the shake test (WHO, 2006). Hasija *et al.* (2013) have reviewed the potential degradation pathways, support analytical methods development, identification of potential vaccine stabilizers and optimal conditions for long-term storage.

It is an alarming situation that only 59.89% and 28.73% refrigerators and freezers, respectively, had suggested storage temperature of vaccines. Moreover, 76.3% had medications in the vaccines' refrigerator/freezer but mainly found in pharmacies. In cumulative vaccine storage refrigerator/freezer, 61.62% contained food, drinks, and 5.05% had even laboratory specimens. It is an awful condition to know that 5.35% refrigerators and/or freezer were only for vaccines. Butt and his co-workers have found that only 50% respondents know about the recommended temperature of vaccines (Butt *et al.*, 2005). Furthermore, the upper, and lower shelves, and door shelves contained water filled bottles were 3.43% and in 87.92% vaccines were kept in door, upper and lower shelves, 3.36% cumulative freezers had ordinary thermometer, while digital thermometer, and data logger was not found. In a study, it has been found that 10% pharmacies had temperature-monitoring device (Butt *et al.*, 2005). As per the rules and guidelines, every respondent stated that vaccines were immediately placed in the refrigerator or freezer on delivery and it had been observed that all vaccines were in their respective packaging carton. A positive sign of inventory showed first expiry first out (FEFO), all respondents followed the rule and above all no expired vaccine have been found in the refrigerator and/or freezer. It has been facilitated by the pharma-industries in Pakistan to return the expired medications to prevent or compensate the loss of proprietor (Hussain and Ibrahim, 2011).

Only 69.88% refrigerator were less than 10 years old, in the mean while, lose detectable sealing 20.49% was observed only in older refrigerators and/or freezers. Older refrigerators were especially likely to have higher temperatures and have detectable seal breaks on the doors. In case of major power failure, 12.4% cumulative had power substitution. Butt *et al.* (2005) have noticed 4% power substitution (Butt *et al.*, 2005) and 14.18% can be managed by icepacks and/or ice trays in case of transported vaccines to individuals or to maintain the temperature in power broke down. Only in clinics and hospital pharmacies broken seal multiple dosing vials 15.45% and 20.31%, respectively, were found.

Collectively 47.76% health associated professions were available. A hope has been raised by knowing that 100% health associated professionals were available in clinics

Table 3: Guidelines for Storage and Handling of Vaccines

1.	There must be continuing education and training programs.
2.	Provide knowledge about the importance of vaccines.
3.	Educate about the storage of vaccines at manufacturer’s recommended temperature.
4.	Install temperature alarm.
5.	Provide information about the degradation of vaccines by heat, light and freezing.
6.	Vaccines destined to be stored in the refrigerator should never be frozen.
7.	Inform about the importance of shake test.
8.	Ensure FEFO policy.
9.	Do not store vaccines and medicines together.
10.	Do not place food or drink stuff in vaccine refrigerator and/or freezer.
11.	Ice packs and ice bags should be used for dispensing of vaccines.
12.	Knowledge about to store and use of diluents for the reconstitution of vaccine (if needed).
13.	Provide information regarding the digital thermometer.
14.	Manage the inventory, record the stock list.
15.	There must be alternate power supply specific for vaccine’s storage compartments.
16.	Keep vaccines in original packing.
17.	The maximum and minimum temperatures reached each day should be recorded this log book.
18.	Temperatures of the refrigerator and freezer should be checked at least twice each day and documented on a temperature log.
19.	Perform daily inspection of storage unit(s).
20.	Vaccine’s refrigerators and/or freezers are ONLY FOR VACCINES.

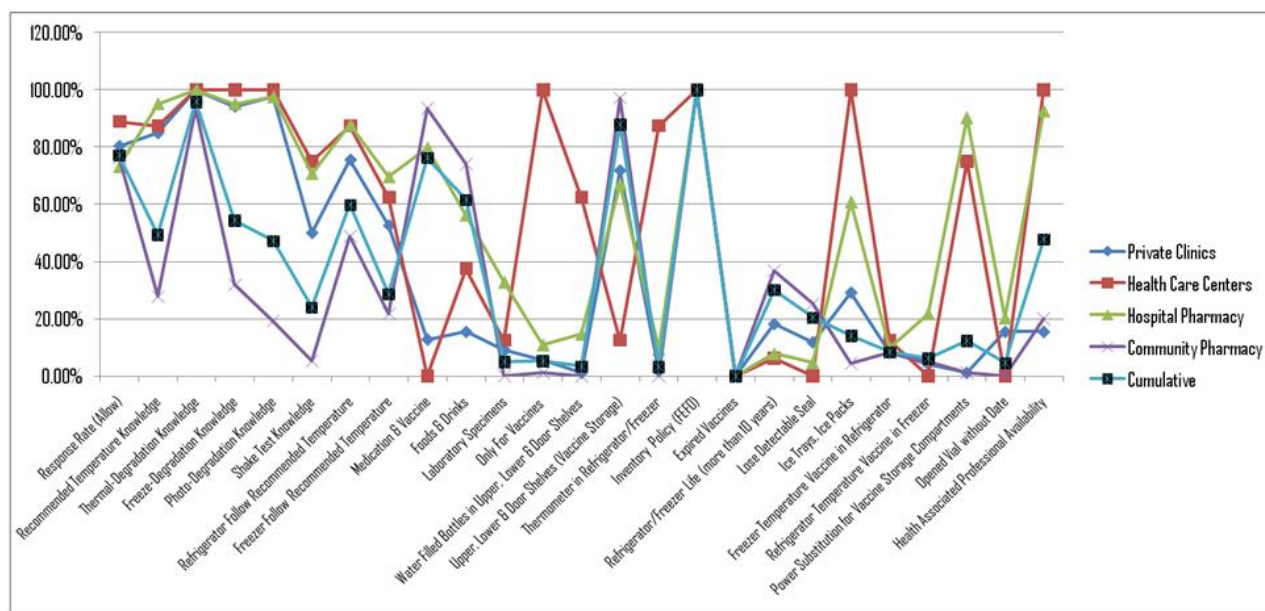


Fig. 1: Respondents Knowledge about Vaccine storage & Handling Errors during Storage of Vaccines

and governmental health care centers, $\geq 92\%$ hospitals pharmacies had pharmacist. It has been found like many developing countries, that the pharmacist were absent or not been involved in community pharmacy (Becklerleg *et al.*, 1999; Saradamma *et al.*, 2000; Rabbani *et al.*, 2001; Syhakhang *et al.*, 2001;). Pharmacist should be in community pharmacy but we had found only 20.08% pharmacist and assistant pharmacist were available. Majority of handling errors were found in community pharmacies due to lack of knowledge regarding storage and handling of vaccines. Food and drinks in vaccine

refrigerators and/or freezers were mainly found in community pharmacies. Water filled bottles in door upper and lower shelves were least found while vaccines were mainly found in these shelves. There was no expired vaccine found due to good inventory control. Major numbers of refrigerators with life more than 10 years old were found with maximum loose detachable seal of doors i.e. the recommended temperature has been least achieved, similarly ice packs and ice trays were lesser in number, mainly in community pharmacy. The main reason of mishandling was the lesser number of health

associated professionals with lack of knowledge, training and economic crisis in community pharmacy.

The desired potency of vaccines is an integral part for vaccination. The potency of respective vaccines varies significantly by change in the recommended storage temperature. By the change in potency, vaccines may not produce the desired preventative assurance. Thus, the present study suggests that all vaccines coordinators should have to strictly follow the proper storage temperature. The problems of proper handling and storage can be minimized by strictly following and implementing the rules of very renowned guidelines like Centers of Disease Control and Prevention, USA (CDC, 2015), Canadian Immunization Guide by Public Health Agency of Canada (PHAC, 2015), storage and handling of vaccines by American Academy of Pediatrics (AAP, 2015), immunization against infectious disease by Public Health, England (Salisbury and Ramsay 2013), National Vaccine Storage Guidelines by Department of Health and Ageing by Australian Government (DoHA, 2013), National Guidelines for Vaccine Storage and Distribution by New Zealand (MoH, 2012) Ontario Public Health Standards by Minister of Health and Long-Term Care, USA (OPHS, 2014), Vaccine Storage Temperature Monitoring Guidelines (DoH) (2015).

It is very unfortunate there is no official guidelines for the storage and handling of vaccines exist in Pakistan. On the basis of present study, we have suggested that some precautionary measurements/guidelines (table 3) must be taken by pharmacies, vaccination centers and health-care centers for proper storage and to minimize the handling errors. The continuing education programs are the most effective way to minimize the errors and to educate about the proper storage and handling of vaccines. It is not only the responsibility of government but also managed and conducted by pharma-industries, healthcare foundations and NGOs.

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