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Basic Study

Healthcare seeking trends in acute respiratory infections among children of Pakistan

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Data sharing statement: Technical appendix, statistical code, and dataset are available from the corresponding author at hyahya82@yahoo.com. Considering this is subanalysis of secondary data obtained through demographic health surveys (DHS), therefore the National Institute of Population Studies collected data after seeking consent from the participants and we

have sought permission from the custodian organization of DHS for data sharing.

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Abstract

AIM

To assess healthcare seeking trends among Pakistani children with acute respiratory infections through comparative analysis between demographic health surveys (DHS) 2006-2007 and 2012-2013.

METHODS

Data of the last born children 0-24 mo of age of the sampled households from both the DHS was analyzed

after seeking permission from the DHS open access website. These were children who had suffered from cough and/or breathing difficulty in the past two weeks and sought health care thereafter. The trends of health care seeking were determined separately for the individual, household and community level according to the study parameters. χ^2 test was applied to compare these trends. A *P*-value of < 0.05 was considered significant.

RESULTS

Out of 2508 children in 2006-2007 there were 1590 with acute respiratory infections (ARI) according to case definition along with 2142 out of 3419 children in 2012-2013 DHS, whose data was analyzed. During 2006-2007, 69% cases sought healthcare for ARI which improved to 79% in 2012-2013. Additionally, it was revealed that when compared between 2006-2007 and 2012-2013, improvement in care seeking practices was observed among illiterate mothers (64% *vs* 77%) although there was minimal change in those literate. Similarly, those women working also showed an increase in healthcare seeking from 67% to 79%. Additionally, those belonging to low and middle socioeconomic class showed a marked increase as compared to those in the higher class where there was no significant change. Whereas those living in rural communities also showed an increase from 66% to 78%.

CONCLUSION

Increasing health budget, improving maternal education and strengthening multi-sectoral coordination are among the effective strategies to improve outcomes associated with healthcare seeking in ARI.

Key words: Acute respiratory infections; Demographic health surveys; Comparison; Pneumonia; Healthcare seeking

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Core tip: Acute respiratory infections (ARI) contribute to childhood morbidity and mortality due to poor healthcare seeking among other causes. We aimed to identify the healthcare seeking trends among Pakistani children with ARI through comparative analysis between DHS 2006-2007 and 2012-2013. Data of last born children 0-24 mo was analyzed. In 2006-2007, 69% cases sought healthcare which improved to 79% in 2012-2013. Improvement was observed among poor, illiterate mothers, those working, and/or living in rural communities. It is therefore, important to develop strategies and interventions focusing on this category of caretakers to improve the outcome associated with ARI.

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INTRODUCTION

Acute respiratory infections (ARI), in general, and pneumonia, in particular, continue to be the leading causes of childhood morbidity and mortality worldwide^[1]. This leads to a substantial burden on the healthcare system and can cause serious complications leading to economic and psychological burden at the household level^[1,2]. According to the World Health Organization (WHO) and United Nations International Children's Emergency Fund, globally, over 2 million children die each year due to ARI with pneumonia^[3] contributing to about one fifth of deaths of children aged less than five years^[4]. Although numerous efforts have been put forth by the global community to combat these infections yet there has been little improvement witnessed in the reduction of the incidence of these diseases globally^[2]. In Pakistan more than 250000 children die each year due to pneumonia^[5,6]. This makes Pakistan enlisted among the top five countries globally with the highest childhood mortality due to pneumonia, a preventable disease^[3,7]. Over 80% of these deaths occur due to lack of adequate and timely healthcare seeking^[2]. It is, therefore, important to seek appropriate health care timely when children develop signs of ARI which include cough accompanied by short rapid breathing^[8].

Studies have documented that delayed health care seeking behavior due to lack of knowledge regarding level of seriousness of the disease are among the leading causes^[9-11]. In a formative research conducted in Nepal, Bangladesh and Pakistan regarding care seeking practices in the rural communities for newborn care, it was found that danger signs were not comprehended by the caretakers, therefore they mostly sought treatment from the local healers, *i.e.*, homeopaths or non-qualified practitioners. Further, the traditional beliefs of influence of evil spirits, lack of understanding and awareness regarding the disease, distance from healthcare facilities, and high cost of treatment are hurdles in healthcare seeking behavior^[12]. In another study conducted in Nigeria regarding the care seeking practices of childhood illnesses, 62% of the cases sought care beyond 24 h after the initiation of illness with 57% dealt with at home^[13]. Another study conducted in Nigeria determining the effects socio-demographic characteristics on care seeking trends showed that high socioeconomic class and high maternal education were the major factors contributing towards early health care seeking from health facility^[14]. In Pakistan, a study conducted to assess the healthcare seeking patterns in diarrhea among uneducated mothers of low resource peri urban Karachi showed that lack of transport and high cost of therapy are the major reasons for not seeking healthcare^[15]. In a similar study

conducted in rural Ecuador, it was found that lack of recognition of the danger signs of acute respiratory illnesses led to delayed care seeking irrespective of the socioeconomic status^[16].

It is, therefore, important to understand the factors leading to poor health seeking behaviors among the caretakers of children suffering from ARI. This can assist in developing effective strategies to improve survival of children under five of developing countries. ARI continues to be among the major health problems in Pakistan, especially when there has been limited evidence generated regarding the health care seeking behavior over the past decade. We aim to assess the trends of the health care seeking behaviors among caretakers of children with ARI especially pneumonia in Pakistan with respect to the demographic health surveys (DHS) conducted during 2006-2007 and 2012-2013.

MATERIALS AND METHODS

Study definitions

Acute respiratory illnesses: The cases of ARI were screened on the basis of children having cough, fast breathing or difficult breathing during the past two weeks according to the DHS questionnaire. These illnesses were divided into those who had "pneumonia" and those with "no pneumonia". Those cases which only had symptoms of cough and fever were labeled as "no pneumonia". Those cases which had fast breathing or difficult breathing due to involvement in the chest were labeled as "pneumonia".

Care seeking: Care seeking was defined as when the caretaker sought advice or treatment for the illness from any source according to the DHS questionnaire. This included all types of care sought, either traditional or formal. It included whether visiting a government or private hospital, private clinics or doctors, Lady Health Workers, homeopath doctor or other primary level healthcare settings. The study outcome was dichotomized as the one who sought care and the one who did not seek care for ARI.

Data source: It is retrospective study whereby secondary data from datasets of 2006-2007 and 2012-2013 Pakistan demographic health survey (PDHS), carried out by the National Institute of Population Studies, was utilized after seeking permission from the Demographic Health Survey Program under US-AID. The survey in both the cases was designed to provide information on maternal and child health. The sampling methodology employed in both the surveys was multistage stratified cluster sampling whereby urban and rural samples were drawn separately. The sample was nationally representative in line with the population distribution in each province of the country. Random household sampling was conducted to select the respondents for the survey. Considering this is a sub analysis of an existing dataset therefore consent

from the participants of the survey was not sought as the National Institute of Population studies had taken prior consent upon completion of the survey. The data set was downloaded from the public access website (<http://www.measuredhs.com>). In the 2006-2007 survey 10023 respondents were surveyed whereas in the 2012-2013 survey the sample was of 12943 respondents. The response rate for the 2006-2007 survey was 94.5% whereas that of 2012-2013 was 93.1%. The data was inspected for quality, completeness of information and comparability of variables required for the present analysis. The variables from the data set were then selected according to the objectives and the files were constructed. We selected lastborn children from 0-24 mo of age at the time of the survey who had suffered from cough in the last two weeks and were living with respondents/mothers. There were 2508 cases identified with history of cough in DHS 2006-2007 whereas 2012-2013 had 3419 such cases. According to the case definition 1590 and 2142 children in DHS 2006-2007 and 2012-2013 respectively with acute respiratory symptoms were finally analyzed.

Statistical analysis

The data was analyzed using STATA 10.0 software. Frequency and percentages were calculated for ARI and its care seeking. The trends of health care seeking were determined separately for the individual, household and community level according to the study parameters. The variables included maternal age, maternal education, working status, father's occupation, child age, gender, residence, place of delivery, delivery conducted by, socioeconomic status and geographical region. These variables were then coded and categorized. χ^2 test was applied to compare the trends of the rates of care seeking among the different categories according to the study parameters. A *P*-value of < 0.05 was considered significant. The statistical methods of this study were reviewed by the biostatistician of Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan.

RESULTS

There were 1590 children with the respiratory symptoms identified during the DHS 2006-2007, of which 1167 (73.3%) had pneumonia and 374 (23.5%) cases had no pneumonia according to case definition. On the other hand, during DHS 2012-2013 there were 2142 children with respiratory symptoms among which 1610 (75.1%) were with pneumonia and 474 (22%) were with no pneumonia. The underlying diagnosis of the rest of the cases in both the surveys was unknown. According to the DHS data, health care for ARI was sought by 1108 (69.6%) cases in 2006-2007 which included 813 pneumonia cases and 295 no pneumonia cases. Similarly 1707 (79.7%) children sought health care in 2012-2013 with 1276 pneumonia and 431 no pneumonia cases (Table 1 and Figure 1).

The majority of ARI cases presented during

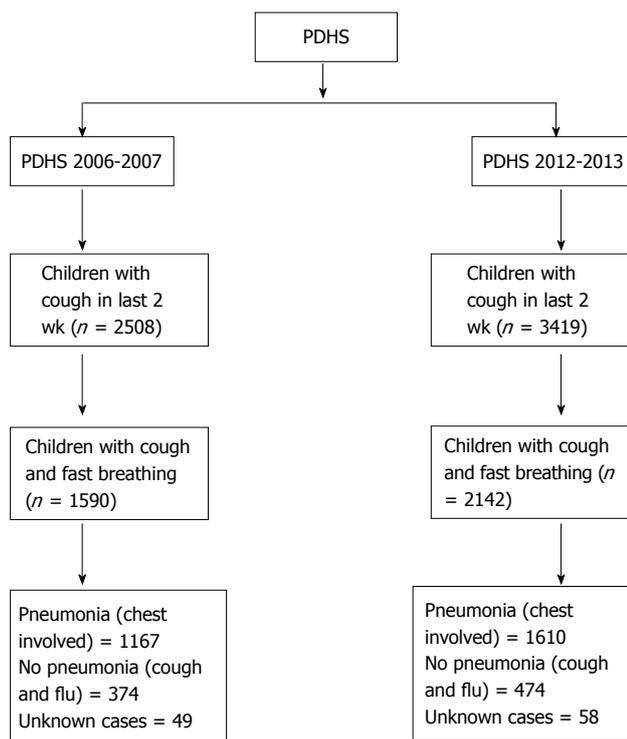


Figure 1 Distribution of children according to different acute respiratory infections categories. PDHS: Pakistan demographic and health survey.

2006-2007 and 2012-2013 were infants aged 1 to 6 mo, *i.e.*, 1213 (76.3%) and 1690 (78.9%) respectively followed by the neonates (< 1 mo). Additionally, male gender was predominantly affected as revealed from both the surveys (Table 2).

According to the statistics, as majority of the cases of ARI are usually diagnosed as pneumonia, therefore further analysis of cases of pneumonia was conducted^[17]. According to the DHS 2006-2007, mothers of younger age group (up to 20 years) were more likely (77.1%) to seek care for their child with pneumonia as compared to the other age groups, *i.e.*, 66.9%. Whereas according to the DHS 2012-2013 the mothers aged up to 30 years were found more likely (82.0%) to seek care as compared to 77.3% of other age groups.

There was increase in healthcare seeking among the illiterate men and women in 2012-2013 as compared to 2006-2007. This rise in healthcare seeking observed among illiterate women was from 64% to 77% whereas that for men was from 59% to 77% between 2006-2007 to 2012-2013. However, the trend in educated caretakers remained static when the average of those with primary, secondary and above educational status was compared in both surveys. It was, however, found that of all the levels of education, those who were educated sought care with a higher proportion as compared to those illiterate.

In DHS 2006-2007 it was noted that the jobless fathers and the ones involved in unskilled work were less likely to seek health care, however, in the DHS survey 2012-2013 fathers' occupation had no influence on variability of care seeking. Similarly, it was observed

Table 1 Prevalence of acute respiratory infections and its care seeking according to Pakistan demographic and health survey data 2006-2007 and 2012-2013, *n* (%)

	PDHS 2006-2007 <i>n</i> = 1590	PDHS 2012-2013 <i>n</i> = 2142
Pneumonia	1167 (73.3)	1610 (75.1)
No pneumonia	423 (26.7)	532 (24.8)
Care seeking for ARI		
Sought	1108 (69.6)	1707 (79.7)
Not sought	482 (30.3)	435 (20.3)

PDHS: Pakistan demographic and health survey; ARI: Acute respiratory infections.

Table 2 Baseline characteristics of children with acute respiratory infections according to Pakistan demographic and health survey data 2006-2007 and 2012-2013, *n* (%)

	PDHS 2006-2007 <i>n</i> = 1590	PDHS 2012-2013 <i>n</i> = 2142
Age		
Neonates (up to 28 d)	377 (23.6)	452 (21.0)
1 to 6 mo	1213 (76.3)	1690 (78.9)
Gender		
Male	877 (55.2)	1143 (53.4)
Female	713 (44.7)	999 (46.5)

PDHS: Pakistan demographic and health survey.

that health care seeking was increased among working women from 2006-2007 to 2012-2013 but was decreased among the non working women from 2006-2007 to 2012-2013 as shown in Table 3.

In 2006-2007, it was found that children delivered at healthcare facilities sought healthcare more than those delivered at home (76.7% vs 65.5%). Those who were delivered by health professionals also sought healthcare more as compared to those born by traditional birth attendants (79.0% vs 58.4%) and the ones delivered by c-section were more likely to seek care during an ARI episode as compared to ones delivered normally (82.2% vs 68.5%). The same findings were observed for data analyzed in 2012-2013 as shown in Table 3. When data of all these variables was compared between 2006-2007 and 2012-2013 it was found that there was a rise in seeking healthcare in 2012-2013 as shown in Table 3.

It was noted that from 2006-2007 to 2012-2013, there was a rise in care seeking among those in lower (60% vs 75%) and middle socioeconomic class (69% vs 82%) whereas that for the higher class remained almost static (82.4% vs 84.9%).

Similarly, caretakers living in urban areas as compared to rural (77.5% vs 66.0%) were more likely to seek care in 2006-2007 with a similar trend in 2012-2013 (82% vs 78%). However, it was noted that those living in rural communities improved care seeking from 2006-2007 to 2012-2013 (66% vs 78%).

It was found that the care seeking behavior

Table 3 Trends of rates of pneumonia care seeking according to Pakistan demographic and health survey data 2006-2007 and 2012-2013, *n* (%)

	PDHS 2006-2007			PDHS 2012-2013		
	Care seeking (<i>n</i> = 813)	No care seeking (<i>n</i> = 354)	<i>P</i> value	Care seeking (<i>n</i> = 1276)	No care seeking (<i>n</i> = 325)	<i>P</i> value
Individual level factors						
Maternal age (yr)						
Up to 20	37 (77.1)	11 (22.9)	0.01	43 (75.4)	14 (24.5)	0.02
20 to 30	421 (71.5)	167 (28.5)		685 (82.0)	150 (18.0)	
31 or above	355 (66.9)	176 (33.1)		548 (77.3)	161 (22.7)	
Maternal education						
Illiterate	515 (64.2)	287 (35.7)	< 0.001	700 (77.1)	208 (22.9)	0.007
Primary	136 (78.6)	37 (21.4)		221 (79.7)	56 (20.2)	
Secondary or above	162 (84.4)	30 (15.6)		355 (85.3)	61 (14.6)	
Father's education						
Illiterate	252 (59.5)	171 (40.4)	< 0.001	390 (77.2)	115 (22.7)	0.004
Primary	151 (74.7)	51 (25.2)		182 (75.8)	59 (24.2)	
Secondary or above	405 (75.7)	130 (24.3)		704 (82.5)	151 (17.5)	
Father's occupation						
Skilled manual	149 (77.2)	44 (22.8)	< 0.001	214 (84.2)	40 (15.7)	0.11
Unskilled manual	168 (65.3)	89 (34.6)		431 (78.1)	121 (21.9)	
Professional/ technical	63 (72.4)	24 (27.5)		123 (78.8)	33 (21.2)	
Agriculture related	151 (62.1)	92 (37.9)		150 (81.1)	35 (18.9)	
Services/ clerical	253 (75.9)	80 (24.1)		319 (79.9)	80 (20.1)	
Did not work	25 (50.0)	25 (50.0)		33 (70.2)	14 (29.7)	
Others	4 (100.0)	0 (0.0)		6 (75.0)	2 (25.0)	
Maternal working status						
Working	182 (67.1)	89 (32.8)	0.3	247 (79.4)	64 (20.6)	0.46
Not working	631 (70.4)	265 (29.5)		1029 (80.1)	261 (20.3)	
Age of child (mo)						
Neonates	205 (74.2)	71 (25.7)	0.03	275 (81.1)	170 (19.8)	0.13
1 to 2	351 (71.8)	138 (28.2)		590 (81.3)	135 (18.7)	
3-6	257 (64.0)	145 (36.0)		411 (76.5)	126 (23.5)	
Gender						
Male	456 (70.7)	189 (29.3)	0.39	686 (80.1)	170 (19.8)	0.63
Female	357 (68.3)	165 (31.6)		590 (79.1)	155 (20.8)	
Place of delivery						
Healthcare facility	326 (76.7)	99 (23.3)	< 0.001	683 (83.4)	135 (16.6)	0.008
Home	485 (65.5)	255 (34.5)		593 (75.7)	190 (24.3)	
Delivery conducted by						
Health professional	331 (79.0)	88 (21.0)	< 0.001	672 (82.2)	146 (17.9)	0.01
Trained birth attendant	247 (71.1)	100 (28.9)		343 (79.5)	89 (20.7)	
Other untrained attendant	229 (58.4)	163 (41.6)		261 (74.5)	89 (25.4)	
Delivery by cesarean section						
Yes	79 (82.2)	17 (17.7)	< 0.001	169 (84.5)	31 (15.5)	0.19
No	734 (68.5)	337 (31.4)		1107 (79.1)	293 (20.9)	
Household level factors						
Socioeconomic status						
Lower class	326 (60.2)	216 (39.8)	< 0.001	524 (75.3)	171 (24.7)	0.005
Middle class	154 (69.3)	68 (30.7)		279 (82.3)	60 (23.6)	
Higher class	333 (82.6)	70 (17.4)		473 (84.9)	94 (15.1)	
Community level factors						
Residence						
Urban	287 (77.5)	83 (22.5)	< 0.001	531 (82.1)	116 (17.9)	0.05
Rural	526 (66.0)	271 (34.0)		745 (78.1)	209 (21.9)	
Geographical region						
Punjab	321 (73.4)	116 (26.5)	< 0.001	401 (87.3)	58 (12.6)	< 0.001
Sindh	332 (78.8)	89 (21.2)		244 (82.4)	52 (17.5)	
KPK	144 (51.4)	136 (48.5)		335 (70.9)	137 (29.0)	
Balochistan	16 (55.1)	13 (44.8)		129 (72.8)	48 (27.1)	
Gilgit Baltistan	-	-		114 (84.4)	21 (15.6)	
Islamabad (ICT)	-	-		53 (85.4)	9 (14.5)	

PDHS: Pakistan demographic and health survey; KPK: Khyber Pakhtun Khwah.

improved among the caretakers belonging to the provinces of Punjab, Khyber Pakhtun Khwah (KPK) and

Baluchistan in 2012-2013 as compared to 2006-2007. Additionally, it was found that is people living in

Punjab and Sindh were more likely to seek care than those living in Balochistan and KPK provinces (73.4% and 78.8% vs 51.4% and 55.1% respectively) in 2006-2007. A similar trend was observed in 2012-2013 survey and details given in Table 3.

DISCUSSION

Our results show that there has been a significant improvement in health care seeking behavior among caretakers in some of the variables from 2006-2007 to 2012-2013. These included illiterate mothers and fathers, working caretakers, children who were born in the healthcare facilities, belonging to middle and lower socioeconomic class and those living in rural community.

The increase in the healthcare seeking among illiterate mothers and fathers could be attributed to two factors. One reason could be the increase in the migration of large proportion of rural population, the majority of which comprises of illiterate individuals, for higher employment and better healthcare opportunities^[18]. Evidence suggests that urban residence provides better opportunities for healthcare seeking as indicated by a study conducted by Kugelman *et al.*^[18], who identified this difference in behavior among urban and rural communities. They indicated that individuals in rural communities had a lower weekly financial budget not only for healthcare but also for transport to a healthcare facility which led to delayed or no healthcare seeking^[19]. Another study conducted in Bangladesh, whereby secondary data analysis of their DHS was conducted also revealed that urban population sought more care than rural one^[20]. Another reason could be improvement of health management systems at the provincial level down to the level of the district and greater financial autonomy based on needs after devolution of the health ministry in 2011 whereby the autonomy for implementation of policies/programs was given to the provinces^[21,22]. This benefitted the people in the form of quality healthcare delivery close to their doorstep^[23]. This might also have led to increased health care seeking practice among the children who were born in health facilities^[24].

Since the healthcare seeking behavior was found to be raised among the working women, it could be attributed to the provision of opportunity in terms of more fiscal space and awareness regarding utilization of health services. This points to improvement in woman's autonomy which has been observed to more among working women^[25]. Autonomy is defined as the woman's ability to act freely and independently. With increase in both formal and informal employment among Pakistani women, they tend to make decisions based on their independent will^[26]. This could be one of the major factors which might have contributed towards improved healthcare seeking among this group of women. This point is also reflected by decrease in healthcare seeking by non-working women. A study conducted in India on healthcare

seeking behavior for antenatal care revealed that non-working women were less likely to seek healthcare as compared to working ones^[27].

Results also show that there was a difference of healthcare seeking among the provinces with caretakers in Punjab and Sindh seeking more health care as compared to Balochistan and KPK. This could also be the result of the devolution due to which the provinces might be moving at a difference pace from each other in terms of implementation of the health programs^[22]. It has been observed that the province of Punjab has been in the forefront due to their emphasis on the health as compared to the other provinces^[22]. If there are some common factors, other provinces can learn from the experience of that province and improve the indicators however, due to geographical SEC and cultural and political variations should be taken into account while doing so.

It was also evident that when compared among the various socioeconomic classes in both surveys, healthcare seeking behavior was improved more in the lower and middle socioeconomic class as compared to the upper class. This again could be attributed to a change in the health systems which have become more accessible at the grass root level. In addition to that as the per capita income of the country has slightly improved therefore the individuals belonging to this class have shown this increase in healthcare seeking trend^[25]. Another reason could increase in the educational level of the middle class women of the society which again points towards their autonomy as indicated earlier

In order to develop strategic policies and programs, it is important that information related to healthcare seeking behaviors and factors determining these behaviors are utilized. The socio demographic context of these behaviors is among the most impactful of all^[28]. It is, therefore, important to develop strategies and interventions to promote appropriate and timely health care seeking behavior for children as in the absence of such interventions, there is a strong likelihood that there will further be an increase for the vulnerable population to suffer even more. Benefits of improving healthcare seeking are tremendous especially in settings where public health services are limited.

Based on these findings the following recommendations are made to influence policy and practice for improving care seeking for children with ARI: Educating the mothers especially in the rural communities and those of the older age group, on picking up the signs of ARI early through community based integrated programs; improving of quality of care and awareness so that care seeking is sought within 24 h of initiation of symptoms; more investment on infrastructure, by increasing the annual health budget, in the public sector making it accessible for the poor community which cannot afford the private sector; multi sectoral approach by enhancing and strengthening coordination among education, planning, health, and communication at the

planning and implementation phases for example by developing safety net programs which could in turn improve the socioeconomic class of the community; More research on the consequences of delay in health care seeking practices and behavior, to decrease or prevent the high costs of illness.

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COMMENTS

Background

Acute respiratory infections particularly pneumonia continue to be the leading killer in under five children in Pakistan, among other developing countries. Poor healthcare seeking practices are a major predisposing factor towards this. There is little evidence whereby trends of healthcare seeking for pneumonia have been assessed over a specific period of time. The authors have, therefore assessed the trends of healthcare seeking for pneumonia from data obtained from two consecutive demographic health surveys (DHS) (2006-2007 and 2012-2013) to determine any differences therein and to suggest suitable recommendations to improve the system.

Research frontiers

It is important to determine trends in healthcare seeking for pneumonia patients to aid in development of effective innovative strategies. Demographic characteristics play an impactful role over healthcare seeking behavior which has not been assessed to that extent in Pakistan, let alone compared between various surveys.

Innovations and breakthroughs

This is the first study to have compared data between two consecutive DHS to assess healthcare seeking trends for children with pneumonia in Pakistan.

Applications

Healthcare seeking trends tend to affect the outcome of pneumonia. It is important for clinical practitioners to understand what factors are contributing to the fatal outcomes in terms of healthcare seeking so that they could undergo tailor made management of patients based on clinical findings. And this is the kind of information which this study has provided. Various strategies can be suggested for different categories of caretakers. Considering majority of cases did not seek healthcare due to lack of knowledge as indicated in this study, therefore illiterate mothers can be educated by developing and using validated standardized tools. Similarly, when a child is born in a facility the mother can be made aware of the potential diseases including pneumonia at the first point of contact of the newborn to the physician. One suggestion could be the linking of these awareness sessions with the standardized immunization program whereby the caretaker's knowledge is reinforced every time the child is immunized by the healthcare provider. Similarly, the vaccination cards could have printed pictorial messages indicating prevention and identification of the signs of pneumonia. If a patient comes from a poor socioeconomic class, the practitioners should counsel the caretakers upon the preventive measures of pneumonia development to avoid further episodes or new episodes in other children of the household. Additionally, those practitioners who are involved at the policy level should emphasize on development of effective strategies to cater to the factors which needs emphasis. Similarly, the results of this study indicate that there is a gap at the community level which can be filled by regular training of the Lady Health Workers who can

manage the early signs and refer the patients for hospital care timely. This can in turn also assist in documentation of cases of ARI coming right from the community level which otherwise is identified through DHS based on recall.

Peer-review

The basic study is well designed and written.

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Atypical manifestation of herpes esophagitis in an immunocompetent patient: Case report and literature review

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Abstract

Herpes simplex virus (HSV) is known to cause esophagitis in immunosuppressed patients; however, it is rarely seen in immunocompetent patients. We present a unique case of HSV esophagitis in a healthy male, without any immunocompromising conditions or significant comorbidities. The patient presented with a two-week history of dysphagia, odynophagia and epigastric pain. Physical exam revealed oral hyperemia without any visible ulcers or vesicles. He underwent esophagogastroduodenoscopy which noted severe esophagitis with ulceration. Esophageal biopsies were positive for HSV. Serology was positive for HSV as well. After initiating treatment with Famciclovir 250 mg 3 times/d, high dose proton pump inhibitor and sucralfate, patient had complete resolution of symptoms at his 2.5 wk follow up appointment. Subsequent workup did not reveal any underlying immune disorders. While HSV is a known causative of esophagitis in the immunocompromised, its presentation in healthy patients without any significant comorbidity is uncommon. Presentation with a systemic viral prodrome further makes this case unique.

Key words: Immunocompromised; Herpes; Esophagitis

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Core tip: Herpes simplex virus (HSV) is known to cause esophagitis in immunosuppressed patients but rarely does it cause esophagitis in immunocompetent patients. We present a unique case of a healthy 43-year-old man who presented with two week course of dysphagia, odynophagia, and epigastric pain. Work up, which included esophagogastroduodenoscopy, revealed severe esophagitis with ulceration and biopsies showed HSV. He was successfully treated with famciclovir.

de Choudens FCR, Sethi S, Pandya S, Nanjappa S, Greene JN. Atypical manifestation of herpes esophagitis in an immunocompetent patient: Case report and literature review. *World J Clin Infect Dis* 2017; 7(3): 46-49 Available from: URL: <http://www.wjgnet.com/2220-3176/full/v7/i3/46.htm> DOI: <http://dx.doi.org/10.5495/wjcid.v7.i3.46>

INTRODUCTION

Herpes simplex virus (HSV) is a known causative agent for esophagitis in the immunocompromised host. However, its presence in immunocompetent and otherwise healthy patients is rare. Patients with esophagitis often presents with concerning clinical features such as odynophagia, dysphagia, and retrosternal pain. Endoscopic visualization demonstrates mid distal esophageal ulcers^[1,2]. Our case report describes a unique case of HSV esophagitis in an immunocompetent, otherwise healthy male host with an unusual prodrome of symptoms.

CASE REPORT

A 43-year-old man with a past medical history of migraines presented with a 10-d history of progressively worsening dysphagia, odynophagia and burning sensation at the epigastric region with radiation to the back. Although the patient denied any oral ulcers, his symptoms were exacerbated by oral intake lasting for several hours which lead to decreased oral intake, weight loss, generalized weakness, and fatigue. He denied any changes in his bowel habits or gastrointestinal blood loss.

The patient reported a recent history of severe chills, a pustule on his face with purulent discharge, diffuse body aches, nausea, vomiting, and arthralgias. He also noted a diffuse erythematous pruritic rash on his back, lower chest and abdomen that worsened over the last week prior to presentation.

Patient was born in North Carolina and had lived in Florida for over 10 years. He denied any known allergies and denied starting any new medications including over the counter medicines or herbal medications. He reported being employed as a state trooper and denied any sick contacts or recent travel. He admitted to a

20-year history of daily alcohol use. Denied any history of smoking or illicit drug use. He did endorse having an affair with a new girlfriend with whom he had oral sex prior to onset of his symptoms.

Physical examination revealed a man in no acute distress. Mild hyperemia was noted in the oropharynx without any lesions on the mucosal membranes. The patient was afebrile, acyanotic, and anicteric. Other systems were unremarkable. No cervical, axillary, or inguinal lymphadenopathy was noted. Skin exam revealed erythematous follicular rash on chest, back and lower abdomen. No insect bites or target rash was noted. Basic labs, including complete blood count and complete chemistry, were unremarkable. He underwent diagnostic testing which resulted in a positive Hepatitis A IgG. Hepatitis B, hepatitis C, human immunodeficiency virus (HIV), monospot, Lyme disease and rapid plasma reagin testing were negative. On complete blood count (CBC), he had white blood cell count of 7.7 with atypical lymphocytes that were reported at 8% of total, which was slightly higher than normal. HSV 1/2 antibody was positive. Blood cultures and urine cultures remained negative. Esophagogastroduodenoscopy (EGD) revealed severe esophagitis with evidence of erosions and superficial bleeding in the mid esophagus (Figures 1 and 2).

Pathology on esophageal biopsy demonstrated mild chronic inflammation with reactive changes and focal intestinal metaplasia along with positive immunohistochemical staining for HSV (Figures 3 and 4). Also, it revealed multinucleated squamous cells with margination of chromatin and molding of nuclei. Stains for cytomegalovirus (CMV) were negative and Grocott methenamine silver stain did not reveal any fungal organisms. Unfortunately, PCR for HSV-1 and 2 on biopsy specimen was reported as HSV-1/2 and no distinction could be made as to whether HSV virus in biopsy specimen was type 1 or 2. The final diagnosis on pathology report for esophageal biopsy was "HSV esophagitis with ulceration".

Treatment with famciclovir 250 mg thrice daily, pantoprazole 40 mg daily and sucralfate was begun. Within three days of treatment initiation, patient felt well enough to be discharged home on the same regimen. He was seen at a follow up visit after two and a half weeks and reported remarkable improvement of symptoms and was able to tolerate all foods with subsequent weight gain.

DISCUSSION

HSV esophagitis is a common pathologic agent in immunocompromised patients who are on chronic immunosuppressive medications as well as patients with underlying neoplasia, organ transplant recipients and HIV infection. Infection in an immunocompetent host has been noted in rare cases and may be secondary to a primary infection or reactivation of a latent infection^[3].

These infections are mostly caused by HSV-1. HSV-2

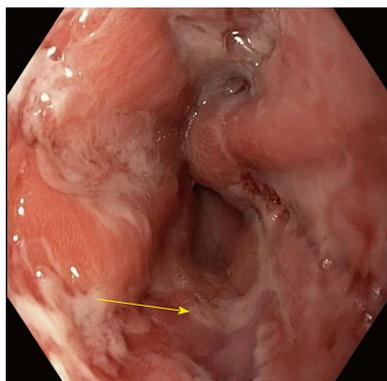


Figure 1 Diffuse ulcerations in the mid esophagus with inflammatory exudate, severe esophagitis 32-42 cm in esophagus.

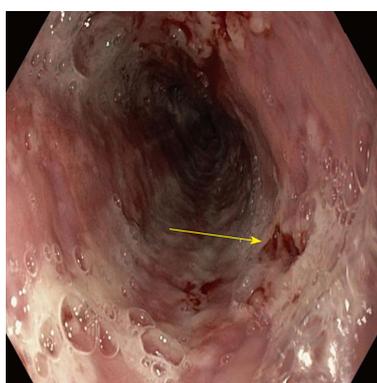


Figure 2 Endoscopic appearance of shallow base ulcers with evidence of erosions and superficial bleeding of the esophagus.

related esophagitis is extremely rare. Traditionally, the first episode of oral-facial HSV infection is caused by HSV-1 with a current rise in oral HSV-2 infections paralleling the change in sexual behaviors^[2]. Also, HSV-1 is becoming a predominant cause of first episode of genital herpes in young adults^[2].

Oral-facial HSV infections caused by either HSV-1 or HSV-2 can be transmitted to heterosexual partner involved in an orogenital contact. With an increasing prevalence of unprotected orogenital sexual contacts, there has been a reported increase in transmission of anogenital infections caused by HSV to the oropharynx resulting in HSV related esophagitis^[2].

We believe that our patient who was recently involved in an orogenital contact with a new girlfriend and may have contracted HSV-1 or HSV-2 infection resulting in infection of his oropharynx by either HSV strain and eventually causing esophagitis.

We performed a review of all available literature on the topic and noted a paucity of data. Patients usually present with typical symptoms of dysphagia, odynophagia, retrosternal discomfort, heartburn, nausea, vomiting, weight loss, cough, and epigastric pain^[3]. Once noninfectious etiologies of esophagitis have been ruled out, the most common etiologies include HSV, CMV and Candida. Other etiologies should be considered

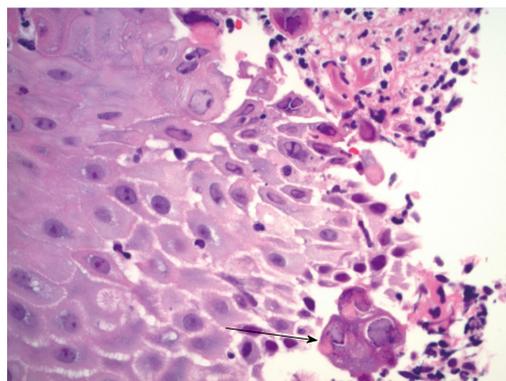


Figure 3 Hematoxylin and Eosin stain showing squamous cells with viral cytopathic effects of herpes simplex virus 1 and 2 - cowdry type A inclusion body- which includes multinucleation, margination of chromatin and molding of nuclei.

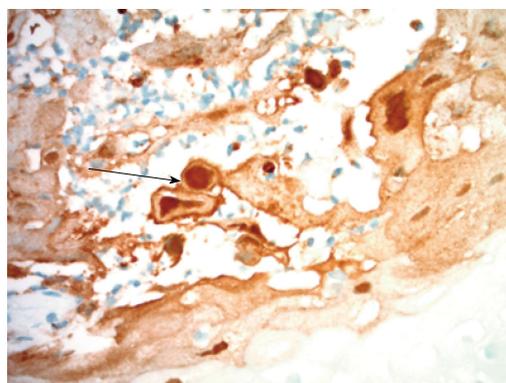


Figure 4 Immunohistochemistry stain for herpes simplex virus 1 and 2 shows the involved nuclei as staining brown for herpes simplex virus viral particles.

in differential diagnosis of esophagitis and these include but are not limited to malignancy, esophageal stricture, reflux esophagitis and eosinophilic esophagitis. HSV is the second most common cause of infectious esophagitis^[4]. It has been described in a wide age range and appears to have a pattern of male predominance with a ratio of 3:1^[1]. Prior exposure to HSV is reported in 20% of cases^[4]. Symptoms are usually characterized by acute onset of odynophagia and epigastric pain in the majority of patients with or without prodromal symptoms. These prodromal symptoms usually consist of fever, malaise, pharyngitis, and upper respiratory symptoms^[5]. Oropharyngeal manifestations (herpes labialis) may be associated and has been reported in 20% of cases^[5].

The distal esophagus is the most common site involved (63.8%) and usually affects with the large portions of esophageal mucosa (92.1%)^[5]. In the early stages of the disease, discrete vesicles can be appreciated; these typically slough off to form circumscribed ulcers. The mucosa is friable and inflamed in most cases (84%) and can be covered with a white exudate. Late stages are characterized by mucosal necrosis^[4]. Biopsies from the edge of ulcers can confirm the disease and such

biopsies usually show cowdry type A inclusion bodies which are very classic for HSV related infections. Although polymerase chain reaction (PCR) is preferred for its high sensitivity (92%-100%) and specificity (100%), cell culture and virus isolation are considered the gold standard^[1,3]. Direct immunofluorescence assays can be applied as a faster diagnostic tool but is limited by a sensitivity of only 69%-88%^[1]. Serology is usually a poor diagnostic tool considering most adults have prior exposure to HSV, however, it can be useful in cases of primary HSV where patients experience seroconversion^[4]. Although, not usually obtained, double contrast radiographic studies can visualize superficial ulcers against a background of normal mucosa^[6]. Ulcers develop a punctate, stellate, or ring like configuration and may be surrounded by radiolucent mounds of edema.

The diffuse rash in our patient was of uncertain etiology. HSV may present with dermatologic manifestations in the form of erythema multiforme^[7]. This is an immune mediated hypersensitivity reaction and in the setting of HSV, presents with oral lesions and a classic targetoid rash and typically resolves with HSV treatment. HSV esophagitis in an immunocompetent host is usually self-limiting and recurrence is rare. Rare complications such as upper GI bleed and perforation of the distal esophagus can occur without treatment^[5].

Benefits of therapy have no clear evidence, although it has been shown to shorten duration of illness by about 6 d^[4]. Due to odynophagia, IV Acyclovir is traditionally the drug of choice which can be then transitioned to oral prodrugs such as famciclovir and valaciclovir. Cases treated with acyclovir showed clinical response in less than 3 d with complete resolution of symptoms within 4-14 d of therapy^[1]. Our case highlights the importance of keeping HSV esophagitis as one of the differential diagnosis for immunocompetent patients who present with symptoms suggestive of esophagitis.

COMMENTS

Case characteristics

A healthy 43-year-old man presented with 2 wk history of dysphagia, odynophagia, and epigastric pain radiating to back that worsened with oral intake.

Clinical diagnosis

Esophagogastroduodenoscopy (EGD) revealed severe esophagitis with evidence of erosions and superficial bleeding in the mild esophagus. Pathology on biopsy was positive for herpes simplex virus (HSV).

Differential diagnosis

With ulcerate lesions in the esophagus and odynophagia, differential is broad and includes infection, malignancy, esophageal strictures, reflux esophagitis, and eosinophilic esophagitis.

Laboratory diagnosis

Gold standard for diagnosis is cell culture and virus isolation but PCR is preferred for its high sensitivity and specificity.

Imaging diagnosis

Esophagogastroduodenoscopy provides direct visualization of the ulcerate lesions that characterize HSV esophagitis.

Pathological diagnosis

Ulcer biopsy can confirm the disease and they usually show cowdry type A inclusion bodies which are pathognomonic for HSV related infections.

Treatment

Therapy has shown to shorten duration of illness and options include intravenous acyclovir or oral famciclovir and valaciclovir.

Related reports

Very few reports exist for immunocompetent patients with HSV esophagitis. It is more common in immunocompromised hosts.

Term explanation

EGD is abbreviation for esophagogastroduodenoscopy.

Experiences and lessons

HSV esophagitis must be kept in the differential when any patient presents with odynophagia regardless of immune status.

Peer-review

This manuscript presents an interesting case and it is well written, organized, and informative.

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