DIAGNOSTIC ACCURACY OF CLINICAL PARAMETERS IN THE DIAGNOSES OF H1N1 INFLUENZA USING PCR AS A GOLD STANDARD

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ABSTRACT

Background: There has been a global outburst of Pandemic H1N1 2009 influenza virus (H1N1) in recent ye Clinical features of respiratory infections can be misleadingly similar but a conglomerate of clinical features may predictive. PCR test is confirmatory but expensive; It is cost effective only if the predictive factors are known.

Objective: The objective of the study is to know about the clinical features which can be predictive of H1N1 influen to enable us to positively diagnose it by PCR in those patients where there is a high suspicion. This would enable to get the maximum benefit from a test which will not be cost effective otherwise

Methods: A retrospective cross-sectional study was conducted in the Swine flu isolation unit of General Medicine Hayatabad Medical Complex, Peshawar, Pakistan. It is a post-graduate institute and tertiary care facility. The stu took place in a time period between November2009 to December2010. All patients with influenza-like illness le than a week duration were studied. The study group included all patients on whom Real Time PCR was perform and were studied retrospectively for the clinical features. A comparison between clinical data and positive a negative PCR was done

Results: There were 284 patients presenting as a flu-like illness. Of those, 102 patients (36% of total) had had a PC test and 37 patients of these (36.3%) had positive PCR test. The four clinical predictors for a positive PCR test we dyspnoea, coryza, headache and fever with the adjusted odds ratio (95% confidence interval) of 4.6429 (2.56 8.4037), 4.6429 (2.5651-8.4037), 6.0341 (3.2613-11.1643), and 2.5097 (1.4274-4.4125), respectively. The specific ity of these four cardinal clinical symptoms is 77% with a sensitivity of 100%. The positive predictive value is 71% wit a negative predictive value of 100% and the accuracy is 85%.

Conclusion: A conglomerate of clinical features can be predictive of H1N1 Influenza and it would help us in reducing the workload on the laboratory especially in resourse poor countries like Pakistan.

Keywords: H1N1 Influenza, Influenza, Swine Flu.

INTRODUCTION

The first case of H1N1 Influenza emerged in Mexico in March 2009[1,2]. Cases were reported in Iran soon afterwards[3] and the first pandemic of Influenza was announced by WHO August 2009[4]. It was such a quick emergence that the medical teams were not ready for the pandemic and little was known about the clinical features and laboratory diagnosis. Serological tests and PCR diagnosis was soon available for the novel H1N1 Influenza virus detection[5].

With the passage of time, the disease has revealed itself and we know much more about the clinical features, diagnosis and treatment of H1N1 Influenza. Influenza like illness (ILI) is such a common disease in the community that if the peculiar features of H1N1 Influenza are not known with good accuracy there would be a great burden on the diagnostic workup of the disease which would exhaust human recourses without adding up much to the diagnostic accuracy.

The objective of the present study is to develop a clinical model with clinical features which may be predictive of H1N1 Influenza enabling us to follow a clinical suspicion with a positive diagnosis with PCR. PCR being an expensive test is certainly not cost effective in resource poor countries and limiting its use only in situations where the suspicion is much high more feasible than ordering it in every patient presenting with flu.

A clinical model must be developed which would enable us in knowing the features suggestive of H1N1 Influenza. Epidemiological evidence like residing in an area from which swine flu has been reported or being the contact of an H1N1 Influenza patient though very important may at times be difficult to know or the patient may not deliver.

METHODS

A retrospective cross-sectional study was conducted in the Medical unit of Hayatabad Medical Complex, a tertiary care facility during November 2009 to December 2010.All patients with influenza-like illness less than a week duration were enrolled. Demographic, clinical data and lab investigations with complete blood count and erythrocyte sedimentation rate

(ESR), liver function test, O_2 saturation, sputum and blood cultures, and radiological findings were all recorded. The study group included only those patients on whom a Real time PCR was performed on their pharyngeal secretions. All patients signed an informed

Table1 1: Baseline characteristics of all patients presenting with a flu like illness

Demographic characteristics	Number (n=284) with percentage
Age in years :	
Mean ±SD	35 ±10
Range	28-45
Smokers:	31(10.9%)
Contact with H1N1:	6(2.1%)
Gender:	
Male:	144(50.7%)
Female:	140(49.3%)

Table 2: Baseline characteristics of hospitalized patients with laboratory-confirmed 2009 pandemic (H1N1) influenza

Demographic characteristics	Number of patients tested (n=287)	Number of PCR positive cases (n=37) with percentage
Age in years:		
Mean		35 ±7SD
Range		28-42 (in years)
Smokers:	31	11(35.5%29.7%)
Contact with H1N1:	6	6(100%16.2%)
Gender:		
Male:	144	14(9.7%)
Female:	140	23(16.4%)

Table 3: The various groups of the patients (n=284)

Total:	284(100%)
No of patients in whom PCR was not done:	182(64%)
No of patients in whom PCR was done:	102(36%)
No of patients in whom PCR was positive:	37(13% of total patients, 31% of PCR)
No of patients in whom PCR was negative	65(23% of total patients, 69% of PCR)

Table 5: Diagnostic accuracy of clinical parameters

		PCR		
		Positive	Negative	Total
Clinical parameter	Positive	37	14	51
	Negative	0	51	51
		37	65	102

Parameter	Estimate	Lower-Upper 95% CIs
Sensitivity	100%	(90.36-100)
Specificity	77.27%	(65.83- 85.71)
Positive Predictive Value	70.59%	(57-81.29)
Negative Predictive Value	100%	(93-100)
Diagnostic Accuracy	85.29%	(77.15-90.88)

Table 4: Clinical presentation of hospitalized patients with laboratory-confirmed 2009 pandemic (H1N1) influenza

Total: / Clinical features:	Dyspnea:	Coryza:	Fever:	Headache:	Sputum	Myalgia	Chest pain	Diarrhoea	Hemoptysis	Altered conciousness
Total:(n=284)	74 (26%)	257 (90.5%)	260 (91.5%)	59 (20.8%)	4 (1.4%)	16: (5.6%)	17 (6%)	4 (1.4%)	2 (0.7%)	4 (1.4%)
No of patients in whom PCR was not done: (n=182)	0(0%)	177 (97%)	181 (99.45%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
No of patients in whom PCR was done: (n=102)	74 (72.5%)	80 (78.4%)	79 (77.45%)	59 (57.8%)	4 (4%)	16: (15.7%)	17 (16.6%)	4 (4%)	2 (2%)	4 (4%)
No of patients in whom PCR was positive: (n=37)	37 (100%)	37 (100%)	37 (100%)	37 (100%)	4 (11%)	16: (43.2%)	17 (46.2%)	4 (11%)	2 (5.4%)	4 (11%)
No of patients in whom PCR was negative: (n=65)	37 (57%)	43 (66%)	42 (64.4%)	22 (34%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)

consent and the study was conducted after the ethical committee was informed about the study and the study was started after the approval from the ethical committee. The author worked as the focal person of the isolation unit of H1N1 Influenza during the whole period of the study.

A nasopharyngeal swab was taken by the author himself. Real Time PCR was done on the pharyngeal secretion samples of these patients according to CDC guidelines. These patients were studied retrospectively for the clinical features. Statistical Analysis was done using SPSS version13.

RESULTS

From November 2009 to December 2010, 284 patients presented as a flu-like illness. The demographic characteristics of these patients are given in Table 1. Table 2 shows the baseline characteristics of hospitalized patients with laboratory-confirmed 2009 pandemic (H1N1) influenza. The various groups of these patients are shown in Table 3. These patients presented with varied clinical features and a group of clinical presentation which is given in Table 4. The specificity, sensitivity , positive and negative predictive values of the clinical features are given in Table 5.

Of those, 102 patients (36% of total) had had a PCR test and 37 patients of these (36.3%) had positive PCR test. The four clinical predictors for a positive PCR test were dyspnoea, coryza, headache and fever with the adjusted odds ratio (95% confidence interval) are 4.6429 (2.565-8.4037), 4.6429 (2.5651-8.4037), 6.0341 (3.2613-11.1643), and 2.5097 (1.4274-4.4125), respectively.

DISCUSSION

Almost all respiratory infections, at least in the outset have similar clinical features and it is quite a difficult task to predict H1N1 Influenza infection without a thorough laboratory workup. This workup is not very cheap and not easily available for this novel Influenza. Being a contact of H1N1 patient or living in an endemic region is easily said than proved. Some patients are in a critical state and others do not give a good history or deny being with an influenza patient. The rapid Influenza tests have low sensitivity[6,7] and the PCR test is not very cost effective.

Influenza like illness and H1N1 are not synonymous and the clinicians must develop a consensus clinical model to have a high index of suspicion for H1N1 influenza while treating Influenza patients. The four cardinal clinical features in our patients were coryza or runny nose, dyspnoea, headache and fever in all our patients. This is in agreement to a very recently conducted study[8]. The adjusted odds ratio (95% confidence interval) of 4.6429 (2.565-8.4037), 4.6429 (2.5651-8.4037), 6.0341 (3.2613-11.1643), and 2.5097 (1.4274-4.4125), for dyspnoea, coryza, headache and fever respectively was against 0·31 (0·12-0·79), 6·25 (1·42-27·49) and 1·69 (1·08-2·66) for coryza, headache and fever of the same study[8]. Dyspnoea, however a cardinal feature of our study was not mentioned as an important factor in that study from Thailand where history of contact was cardinal with an Odds ratio of 2·84 (1·09-7·40) at 95% CI.

Another recent study does not agree to the clinical model which states that clinical signs cannot reliably differentiate H1N1 positive patients[9]. These researchers have however found a higher proportion of patients presenting with myalgias turning out to be H1N1 positive on PCR. Another study about the clinical and radiological features of H1N1 Influenza also refutes any difference in the clinical and radiological features of H1N1 Influenza positive and negative cases[10].

CONCLUSION

The clinical model of H1N1 Influenza proposed earlier and which is apparently proposed by our study also is incomplete and a more detailed insight into the matter must be undertaken. There should be a high index of suspicion in cases presenting with fever, dyspnoea, coryza and headache in previously healthy individuals especially in Influenza season and though the degree of danger has abated for H1N1 Influenza it is not altogether gone and resurgence with yet another other novel mutant may be underway. In appropriate setup PCR should be done judiciously in patients with high suspicion. Further studies are required and retrospectively all record should be checked in units set up for the H1N1 pandemics.

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