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Original Research Article

Comparison of haematological profile in influenza A H1N1 positive and negative patient

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ABSTRACT

Re-emergence of infectious diseases are commonly seen with viral infections among which those caused by Influenza viruses are by nature unstable and unpredictable because of the unique capability of changing their antigenic characteristics by mutation. This study aims to unravel the haematological consequences of Influenza A H1N1 infections and also to compare it with Influenza A H1N1 negative infections.

Materials and Methods: Applying the relevant inclusion and exclusion criterion yielded a total hundred patients consisting of sixty-five Influenza A H1N1 positive and thirty-five Influenza A H1N1 negative patients. The CBC profile of all these subjects were obtained from an Automated hematology analyzer which yielded various haematological parameters.

Results: The mean hemoglobin was 12.145 gm/dl in H1N1 positive cases and 12.6 gm/dl in H1N1 negative cases. The mean hematocrit value was 36.28% in H1N1 positive cases and 40.65% in H1N1 negative cases. 26 H1N1 positive cases had leucopenia, whereas 4 H1N1 negative cases had leucopenia and 8 H1N1 positive cases had leucocytosis. Lymphopenia was observed in 60% of H1N1 positive cases and in 22.9% H1N1 negative cases. Thrombocytopenia was a feature in 8 H1N1 positive cases and 2 H1N1 negative cases.

Conclusions: Several haematological variations are observed in both H1N1 positive cases and H1N1 negative influenza cases, but to different extents.

1. Introduction

The re-emergence of various viral infections that exhibit increased virulence, an aggressive behaviour and showing a propensity for rapid spread are more common now than what was seen in the past. Influenza caused by influenza type A or B virus occuring in outbreaks of varying severity almost every winter is an acute febrile illness.[1]

The unique capability of changing their antigenic characteristics by mutation makes the Influenza viruses unstable and unpredictable. During the spring of 2009, triple re-assortment lead to the emergence of a Novel Influenza A H1N1 virus in Mexico and the USA. In April 2009, the WHO declared a public health emergency of international concern, raised the pandemic alert to 6 on June 2009, indicating that a new influenza pandemic was underway.[2]

The symptoms range from mild upper respiratory symptoms to acute respiratory distress syndrome requiring mechanical ventilations, and even death. Individuals with comorbidities such as diabetes, asthma, heart disease, or immunosuppression and with young adults or children, pregnant women, nursing home residents considered at increased risk.[3]

The Centre for disease control (CDC) recommended rapid diagnostic tests for all suspects and prioritized confirmation by rRT-PCR for hospitalized patients with treatment being initiated without awaiting test results. While in countries like India, UK and other European countries testing done in severe cases (category C) by rRT- PCR and

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treatment given for the severely ill and high risk cases.[4–6]

Sufficient clinical research outcomes enable rapid detection, investigation and characterization of clinical syndromes and enabling effective combatting of such diseases with pandemic potential.[7]

Preferential involvement of certain high risk groups, the unclear virulence of influenza A H1N1 virus conflicting strategies to tackle the outbreak make it essential to study and document the various relevant aspects of the disease.

2. Materials and Methods

Patients with influenza like illness, admitted to the attached hospitals of J.J.M. Medical College and other medical centres in Davangere (Karnataka) were involved in this prospective study. The study went ahead with obtaining the ethical clearance from the institutional ethics committee, and informed consent from the participants. After complete clinical examination, patients with clinical features of Influenza like illness were enrolled and relevant investigations done and documented in the proforma.

The inclusion criteria adopted for this study were - positive cases of influenza A H1N1 and negative cases without specific diagnosis. All other Influenza like illness patients with specific diagnosis other than influenza A H1N1 were excluded from the study group.

A total hundred patients consisting of sixty-five influenza A H1N1 positive and thirty-five influenza A H1N1 negative patients formed the study group.

Rapid influenza antigen screening test using SD BIOLINE influenza antigen test kit in clinically directed cases and throat swab rRT-PCR in category C sent to department of Virology, NIMHANS, Bangalore through the DSO were the specific tests done.

The CBC profile of every patient was obtained from Automated Hematology Analyzer ABX MICROS OT18 (ABX HAEMATOLOGIE MONTPELLIER Cedex 04). Hemoglobin, Haematocrit, Total leucocyte count, Relative and absolute lymphocyte count and platelet count parameters were analysed.

3. Results

Table 1 provides the haemoglobin status in our study groups. Hemoglobin values ranged from 7.4 gm/dl to 16.1 gm/dl in Influenza A H1N1 cases with majority patients having their hemoglobin values in the range 12-14 gm/dl and mean hemoglobin being 12.145 gm/dl. In Influenza A H1N1 negative cases, hemoglobin values ranged from 5.4 gm/dl to 14.5 gm/dl with a mean hemoglobin value 12.6 gm/dl and majority patients had their hemoglobin between 12-14 gm/dl.

Table 2 Haematocrit values in Influenza A H1N1 positive cases ranged from 24.5% to 48.3% with majority of the patient hematocrit values in the range of 36-42%. The mean hematocrit value was 36.28%. In Influenza A H1N1 negative cases Hematocrit values ranged from 17.1% to 43.3% with a mean hematocrit value 40.65%. and majority of the patients' hematocrit ranged 36-42%.

Table 3 gives details of Total Leucocyte count, which in Influenza A H1N1 positive cases ranged from 1.4×10^3/ mm^3 to 19×10^3/ $mm^3$and in Influenza A H1N1 negative cases ranged from 2.6 $\times10^3$ to 19.8 $\times10$/ mm^3 Majority of the positive patients had their count in the range of $4\times10^3/mm^3$ - $8\times10^3/mm^3$ with a Mean leucocyte count of $5.77\times10^3/mm^3$. 27 positive cases had leucopenia and 8 positive cases had leucocytosis. [3]. Majority of the negative patients had their count in the range of 4×10^3 -8 $\times10^3/mm^3$ with a Mean leucocyte count of 8.58 $\times10^3/mm^3$. Referring to the normal values for the age, 4 negative cases had leucopenia and 8 negative cases had leucocytosis.

Table 4 gives the lymphocyte percentage, which in positive cases ranged from 3%-36% and in negative cases ranged from 6.2%-42.8%. Mean lymphocyte percentage was 19.04% in positive cases and 25.73% in negative cases. While 36positve cases had values less than 20%.

Table 5 The range of absolute lymphocyte count was 0.1×10^3/cumm-3×10^3/cumm in positive cases and 0.4×10^3-$7.2\times10^3/mm^3$in negative cases. Mean lymphocyte percentage was 1.03×10^3/cumm in positive cases and $2.24\times10^3/mm^3$ in negative cases. As per the age, 39(60%) positive patients and 8 negative cases had lymphopenia.

ives the platelet count, which in positive cases ranged from 20×10^3-$286\times10^3/mm^3$. Mean platelet count was $188.37\times10^3/mm^3$. Eight (12.3%) cases had thrombocytopenia. In case of negative patients the platelet count ranged from 69×10^3/cumm-412×10^3/cumm. Mean platelet count was 197.94 $\times10^3$/cumm. Two (5.7%) cases had thrombocytopenia.

4. Discussion

The hemoglobin status of patients who were influenza positive in our study on an average was 12.1g/dl. The mean value of hemoglobin were 12.4g/dl and 13.8g/dl in studies done by Unal et al.[8] and Chan et al.[9] respectively with values being in normal range. Whereas mean hemoglobin value in cases who were influenza negative in our study was 12.6g/dl in comparison to 13.7g/dl by Chan et al.[9] in Singapore.

In our study, twenty-two(34%) out of sixty-five influenza positive cases had hematocrit values less than thirty-five when compared to eight(26%) out of thirty cases in a study by Louie et al.[10]

In Influenza positive cases leucopenia was demonstrated in 26 (40%) in our study, 26 (11.6%) cases in Mu YP et al.[11] and 59 (20%) cases in Chudasama et al.[12] studies with values less than 4 $\times10^3$/dl. Whereas leucocytosis with values >11×10^3/dl was seen in 8 (12.3%) in our study, 44(18%), 52 (22%), 10(33.3%) in studies done

Table 1: Hemoglobin values

	Positive cases		Negative cases	
Hb	Number of cases	Percentage	Number of cases	Percentage
<8	1	1.5	1	2.9
8-10	2	3.1	2	5.7
10-12	20	30.8	4	11.4
12-14	36	55.4	20	57.1
14-16	5	7.7	8	22.9
>16	1	1.5	-	-
Total	65	100	35	100

Table 2: Haematocrit values

	Positive cases		Negative cases	
HCT	Number of cases	Percentage	Number of cases	Percentage
<24	-	-	1	2.9
24-30	3	4.6	1	2.9
30-36	24	36.9	6	17.1
36-42	33	50.8	21	60
42-48	4	6.2	6	17.1
>48	1	1.5	-	-
Total	65	100	35	100

Table 3: Total leucocyte count values

	Positive cases		Negative cases	
TLC(10^3/cumm)	Number of cases	Percentage	Number of cases	Percentage
<4	26	40	4	11.4
4-8	27	41.5	15	42.9
8-12	4	6.2	9	25.7
12-16	7	10.8	4	11.4
16-20	1	1.5	3	8.6
Total	65	100	35	100

Table 4: Relative lymphocyte count values

	Positive cases		Negative cases	
Lymphocyte %	Number of cases	Percentage	Number of cases	Percentage
<20	36	55.4	6	17.1
20-30	24	36.9	18	51.4
30-40	5	7.7	10	28.6
>40	-	-	1	2.9
Total	65	100	35	100

Table 5: Absolute lymphocyte count values

	Positive cases		Negative cases	
Lymphocyte	Number of cases	Percentage	Number of cases	Percentage
<1	39	60	8	22.9
1-2	21	32.3	8	22.9
2-3	5	7.7	12	34.2
>3	-	-	7	20
Total	65	100	35	100

Table 6: Platelet count values

	Positive cases		Negative cases	
Platelet	Number of cases	Percentage	Number of cases	Percentage
<150	8	12.3	2	5.7
150-250	49	75.4	29	82.9
250-350	8	12.3	2	5.7
>350	-	-	2	5.7
Total	65	100	35	100

by Jain et al.,[13] Skarbiniski et al.[14] and Louie et al.,[10] respectively. There are many reports stating that in the course of viral infections, cytopenias particularly leucopenia and thrombocytopenia may develop due to autoimmune inhibition and/or inhibition at the level of precursor cells in the bone marrow. There are few reports stating that the new influenza A (H1N1) may cause cytopenias.[10]

The mean leucocyte count in influenza negative cases, in our study (8.6×10^3/ mm^3) and in a study done by Chan et al.[9] (7.2×10^3/ mm^3), was within normal range but was mildly elevated 12.8×10^3/ mm^3 in a study done by Zargoulidis et al.[15]

Relative lymphocyte count of <20% was seen in 32.6% and 55.4% of positive cases in study done by Mu YP et al.[11] and our study respectively. Lymphopenia based on the absolute lymphocyte count was seen in 39 (60%) out of 65 influenza positive cases in our study while it was obsereved in 30% of cases in studies done by Louie J et al.[10] (9 of 30 cases), and 33% of cases in Ong AK et al.[16](33 of 100 cases) study. Nichols and collaborators proposed several mechanisms to explain influenza-induced lymphopenia: Lymphopenia could be the result of cell migration from the circulation and/or cell death caused by necrosis or by apoptosis through suppression of hematopoeisis. Apoptosis after exposure to influenza A virus could be a result of virus induced cytokine stimulation or viral induction of Fas. In addition, increased natural killer cell activity in the periphery may be reflective of increased NKC activity in the lung.[17] In our study 22.9% of influenza negative cases had lymphopenia, while 16% cases had lymphopenia in a study done at Singapore by Ong et al.[16]

Thrombocytopenia (values $<150\times10^3$/mm^3) was noted in 33(14%), 49(22.9%), 55(24%), 5(12.3%) cases in studies done by Jain et al.[13] Chudasama et al.,[12] Skarbinski et al.[14] and Louie et al.[10] cases respectively. 8 (12.3%) influenza positive cases in our study demonstrated thrombocytopenia. Whereas in influenza negative cases thrombocytopenia was seen in 2 cases in our study.

5. Conclusion

The mean hemoglobin was 12.145 gm/dl in H1N1 positive cases and 12.6 gm/dl in H1N1 negative cases. Haematological abnormalities like leucopenia, leucocytosis, lymphopenia and thrombocytopenia were noticed to variable degrees in H1N1 positive and H1N1 negative cases.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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