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3 **Is anemia frequent in HIV/AIDS patients presenting to a tertiary**
4 **care hospital?**

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6 **Nauman Ismat Butt¹, Nouman Tehseen², Tashia Malik³, Aniq Anser**
7 **Tufail Khan Kakar⁴, Fahmina Ashfaq⁵, Ayesha Nouman⁶**

8 **1** Department of Medicine, Chaudhary Muhammad Akram Teaching and Research Hospital,
9 Azra Naheed Medical College, Lahore, Pakistan; **2,3,6** Medical Unit II, Jinnah Hospital,
10 Lahore, Pakistan; **4,5** Department of Medicine, Azra Naheed Medical College, Lahore,
11 Pakistan

12 **Correspondence:** Nauman Ismat Butt. **Email:** nauman_ib@yahoo.com

13
14 **Abstract**

15 **Objective:** To determine the frequency of anaemia among patients with human
16 immune-deficiency virus / acquire immunodeficiency syndrome.

17 **Methods:** The descriptive cross-sectional single-blind study was conducted at
18 Jinnah Hospital, Lahore, Pakistan, from June 25 to December 25, 2016, and
19 comprised human immune-deficiency virus / acquire immunodeficiency
20 syndrome patients diagnosed at least 3 months earlier.. Demographic
21 information was obtained along with sample of patient's blood for haemoglobin
22 level estimation. Anaemia was defined as haemoglobin <13 g/dL in males and
23 <12 g/dL in females. Data was analysed using SPSS 20.

24 **Results:** Of the 230 patients, 100(43.7%) were females and 130(56.5%) were
25 males. The overall mean age was 37.99+/-14.48 years. The mean haemoglobin
26 level was 11.08±2.44 g/dl; 113(49.1%) 8-12 g/dl, 26(11.3%) <8g/dl, and
27 91(39.6%) >12g/dl. Overall, 152(66.1%) patients were anaemic and 78(33.9%)

28 were normal. Age and socioeconomic status were significantly associated with
29 anaemia status ($p < 0.05$).

30 **Conclusion:** Anaemia was a common finding among human immune-
31 deficiency virus / acquire immunodeficiency syndrome patients.

32 **Key Words:** HIV/AIDS, Anaemia.

33

34 **Introduction**

35 The human immunodeficiency virus (HIV) is part of the Lentivirus¹ genus
36 member of the Retroviridae family. Lentivirus is transmitted as an enveloped
37 positive-sense single-stranded ribonucleic acid (RNA) virus. After entry into the
38 host cell, the RNA viral genome gets reverse-transcribed into a double-stranded
39 deoxyribonucleic acid (DNA) using the virally encoded reverse
40 transcriptase which gets transported alongside the viral genome into the virus
41 particle. The resultant viral DNA is transferred into the nucleus where it gets
42 integrated into the host DNA using a virally encoded integrase and cellular co-
43 factors.² After integration, the virus can remain latent, therefore premising the
44 virus and the infected target cell to remain undetected by the host's
45 immunologic system. On the other hand, the virus might get transcribed to
46 produce new RNA genomes along with viral proteins which are packaged and
47 then secreted from the host cell as fresh virus particles which commence the
48 viral replication cycle again.²

49 HIV and acquired immunodeficiency syndrome (AIDS) represent a new-age
50 global pandemic. In 2014, worldwide about 37 million people were HIV-
51 positive, and the incidence of newly diagnosed infections was almost 2 million.³
52 However, the number was down from 3.1 million newly diagnosed patients in
53 2001. Out of the 37 million cases, females comprised more than half of the
54 cases and 2.6 million cases were aged < 15 years.³ It caused approximately
55 1.2 million deaths in 2014, which was a reduction from 2.2 million deaths in
56 2005. Sub-Saharan Africa is the most drastically affected region. In 2010,

57 approximately 68% (22.9 million) of the total HIV patients and 66% of all HIV
58 deaths (1.2 million) happened in that region. The second most affected region
59 was south and southeast Asia where in 2010 approximately 4 million cases
60 were reported, representing 12% of worldwide HIV cases, causing an estimated
61 250,000 deaths. About 2.4 million of South Asian patients were in India.⁴ In
62 2008, about 1.2 million individuals in the United States (US) were infected with
63 HIV, causing about 17,500 deaths. It was reported by the Centre for Disease
64 Control and Prevention (CDC) that 20% of the infected individuals in the US
65 were unaware of their HIV status in 2008.³ Frequency was lowest in the Middle
66 East and northern Africa at <0.1%. It was 0.1% in eastern Asia and 0.2% in the
67 western and central Europe. The European countries most affected in 2009 and
68 2012 were Russia, Ukraine, Latvia, Moldova, Portugal and Belarus, in
69 decreasing order of estimated frequency.⁴

70 HIV is a health concern on the rise in Pakistan, with the number of new cases
71 still growing. Recreational drug abuse and extra-marital sex have resulted in the
72 HIV/AIDS epidemic, mostly among the injectable drug abusers, male and
73 female sex workers, and repatriated migrant workers.⁵ The National AIDS
74 Programme shows that more than 17,224 HIV cases have been diagnosed since
75 1986, but the United Nations (UN) and government estimates report the burden
76 of HIV/AIDS cases to be about 97,000 varying from a low value of 46,000 to
77 the high value of around 210,000.⁶

78 The particular details of HIV infection that lead to AIDS have not been yet
79 wholly understood in spite of substantial advances in the virology of HIV and
80 the immunology of the human host.⁷ It is known that HIV causes a reduction in
81 the cluster of differentiation 4+ (CD4⁺) helper T cell counts, with a resultant
82 inversion of the normal CD4/CD8 T-cell ratio along with dysregulation in the
83 production of antibodies by the B-cells. Therefore, immune reaction in response
84 to certain antigens start to deteriorate, and, therefore, host cells do not

85 considerably react, causing increased susceptibility to various opportunistic
86 infections and the normal harmless commensal organisms.

87 Anaemia is often a complication present with infection of the human
88 immunodeficiency virus (HIV), and may be important clinically. The study
89 conducted in Iran⁸ showed the frequency of anaemia of 71%. A study conducted
90 in South India⁹ reported anaemia to be 69% in HIV-positive patients. In Iran¹⁰
91 anaemia was found in 46% subjects.

92 The current study was planned to determine the frequency of anaemia among
93 patients with HIV/AIDS at an urban healthcare facility.

94

95 **Material and Methods**

96 The descriptive cross-sectional single-blind study was conducted at Jinnah
97 Hospital, Lahore (JHL), Pakistan, from June 25 to December 25, 2016, and
98 comprised HIV / AIDS patients diagnosed at least 3 months earlier. Anaemia
99 was defined as haemoglobin (Hb) level <13g/dL in males and <12g/dL in
100 females. Hb level >8g/dl was labelled mild anaemia and <8g/dl as severe
101 anaemia. HIV/AIDS was considered positive using the enzyme-linked immuno-
102 absorbent assay (ELISA) technique and confirmed by the Western blot test.

103 After approval from the institutional ethics committee, the sample size was
104 calculated while keeping confidence interval (CI) of 95% with confidence limits
105 of 6%. The sample was raised using non-probability consecutive sampling
106 technique. Data was collected after taking informed consent from the subjects.

107 Demographic information, like age, gender, address, socioeconomic status
108 (SES) etc., was noted. A 2ml blood sample was taken in **complete blood count**
109 (CBC) vial for Hb level estimation. Single-blind was applied to reduce bias by
110 assigning serial number in place of patient name. Hb level and final outcome
111 anaemia were recorded. Patients with anaemia were managed as per the hospital
112 protocol.

113 Data was analysed using SPSS 20. Mean and standard deviation (SD) were
114 calculated for quantitative variables, like age, duration of HIV/AIDS, Hb level.
115 Frequency and percentage were calculated for qualitative variables, like gender,
116 SES, and anaemia. Effect modifiers, like age, gender, SES, duration of HIV,
117 were controlled through stratification. Chi-square test was applied after
118 stratification by taking $p \leq 0.05$ as significant.

119

120 **Results**

121 Of the 230 patients, 100(43.7%) were females and 130(56.5%) were males. The
122 overall mean age was 37.99 ± 14.48 years (Table 1). The mean Hb level was
123 11.08 ± 2.44 g/dl; 113(49.1%) 8-12 g/dl, 26(11.3%) < 8 g/dl, and 91(39.6%)
124 > 12 g/dl. Overall, 152(66.1%) patients were anaemic and 78(33.9%) were
125 normal. Among the anaemic, 62(41%) were females and 90(59%) were males.

126 In SES terms, 103(44.8%) patients belonged to low SES earning $< 10,000$ rupees
127 per month, 91(39.6%) were earning Rs.10-50,000 and 36(15.7%) were earning
128 $> 50,000$ rupees (Table 2).

129 Mean duration of disease was 11.72 ± 7.96 months, with 71(30.9%) patients
130 having been diagnosed > 12 months ago (Table 3).

131 Age and socioeconomic status were significantly associated with anaemia status
132 ($p < 0.05$), while gender and duration of disease were non-significant ($p > 0.05$).

133

134 **Discussion**

135 Anaemia is often a complication present with HIV infection, and may be
136 important clinically. Causes of anaemia can be multifactorial. By defining
137 anaemia as Hb < 12 g/dL in females and < 13 g/dL in males, the current study
138 showed frequency of anaemia at 66.1% which is slightly less than the 71%
139 reported from Iran⁸. However, the findings of the current study are similar to
140 studies conducted in the region^{9,10}.

141 We observed that anaemia was more frequent in men than women, which is in
142 contrast to some studies^{11,12,13}, but similar to a study that had 9690 HIV-infected
143 patients¹⁴.

144 Frequency of anaemia was about 70% in patients belonging to middle class and
145 68.9% in lower class patients. The high frequency of anaemia in these SES
146 classes points to multifactorial aetiologies of anaemia, including nutritional
147 deficiencies, besides the HIV infection. Better lifestyle and provision of
148 resources may be a factor of low anaemia frequency in high SES. In the current
149 study, mild anaemia was found in 49.1% and severe anaemia in 11.3% subjects.
150 A study in Iran¹⁰ found the presence of mild anaemia in 46% subjects but no
151 case of severe anaemia was observed. Also in Iran, Jabbari et al.¹³ reported the
152 frequency of severe anaemia as 8% (100 patients).

153 In our study, frequency of anaemia was 70.1% in patients diagnosed 6-12
154 months ago, and 67% in patients who had disease duration >12 months. This is
155 in agreement with other studies¹⁵.

156 Anaemia is also an independent predictor of disease progression and mortality,
157 therefore close monitoring for anaemia should be done for patients on
158 zidovudine-based antiretroviral therapy (ART) regimen. Anaemia screening,
159 coupled with anaemia prevention techniques and treatment when required,
160 should be a part of HIV care. A peripheral smear provides information
161 regarding morphology of blood cells and can also provide clues about the cause
162 of the abnormalities in haematopoiesis. However, a study¹⁶ suggested that pre-
163 treatment severe anaemia, as defined by Hb level ≤ 8 g/dL, should not be applied
164 as criteria to avoid the prescription of zidovudine-based ART therapy in limited-
165 resource settings. Cost-effective and prompt screening programmes for anaemia
166 and infectious diseases, along with modification of strategies for morbidity and
167 mortality reduction, are basic requirements in the treatment of HIV/AIDS
168 patients in Pakistan.

169

170 **Conclusion**

171 Baseline anaemia at the time of diagnosis was found to be common in
172 HIV/AIDS patients. Screening and timely management of anaemia are
173 important steps to decrease the severity and overall mortality of the disease.

174

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178

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231 **Table 1: Stratification of outcome with regards to age distribution**
 232 **(n=230)**

Age (years)	Anaemia		Total
	Present	Absent	
18-26	32	25	57
27-35	31	24	55
36-44	32	18	50
45-53	32	7	39
54-62	9	3	12
63-71	8	1	9
72-80	8	0	8
Total	152	78	230

233

Chi square p value: 0.014 (significant)

234

235

236

237 **Table 2: Stratification of outcome with regards to socioeconomic status**
 238 **distribution**
 239 **(n=230)**

Socioeconomic Status	Anaemia		Total
	Present	Absent	
High	17	19	36
Middle	64	27	91
Low	71	32	103
TOTAL	152	78	230

240

Chi square p value: 0.033 (significant)

241

242 -----

243

244 **Table 3: Distribution of Duration of Disease**245 **(n=230)**

Duration of disease (months)	No. of patients	%
3-6	72	31.3
7-12	87	37.8
Greater than 12	71	30.9
Total	230	100.0

246 **Mean duration of disease \pm SD: 11.72 \pm 7.96**

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