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Fanconi Anemia in Egyptian Children: High Consanguinity, Congenital Anomalies, and Bone Marrow Failure in a Tertiary Center Cohort

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ABSTRACT

Background: Fanconi anemia (FA) is a rare inherited bone marrow failure syndrome marked by chromosomal instability, congenital anomalies, and progressive pancytopenia. Early diagnosis is crucial due to increased risk of hematologic malignancies and multi-system involvement, particularly in populations with high rates of consanguinity.

Objective: This study aimed to describe the clinical characteristics and disease outcomes of pediatric patients with Fanconi anemia managed at a single tertiary care center in Egypt.

Patients and methods: A retrospective review was conducted on medical records of 46 children diagnosed with FA between January 2005 and December 2021 at the Pediatric Hematology Clinic, Ain Shams University Children's Hospital. Diagnosis was confirmed by clinical features and chromosomal breakage analysis using diepoxybutane (DEB). Demographics, clinical presentation, laboratory data, bone marrow findings, cytogenetics, treatments, and outcomes were analyzed.

Results: Among the 46 patients, 65.2% were male, and 84.4% had parental consanguinity. Recurrent infections were documented in 43.5%, with no cases of acute myeloid leukemia at diagnosis. Somatic anomalies included microcephaly (58.7%), short stature (55.8%), and skin pigmentation (47.8%). Bone marrow hypocellularity was present in 95% of cases (n=40/42), while dysplastic changes were seen in 20.5% (n=9/44). Cytogenetic analysis revealed a 1q+ abnormality in 2.2% of patients.

Conclusion: This study highlighted the high burden of congenital anomalies and bone marrow failure among Egyptian children with FA, compounded by high consanguinity rates. These findings underscored the need for early diagnosis, genetic counselling, and access to curative therapies like stem cell transplantation.

Keywords: Fanconi anemia, Bone marrow failure, Pediatric hematology, Chromosomal instability, Egypt.

INTRODUCTION

Fanconi anemia (FA) is a rare inherited bone marrow failure syndrome characterized by chromosomal instability, congenital malformations, progressive pancytopenia, and a predisposition to malignancies, particularly acute myeloid leukemia (AML) and solid tumors. It follows an autosomal recessive or X-linked inheritance pattern and is caused by mutations in genes involved in the DNA damage response pathway. Clinical presentation can be highly variable, ranging from subtle physical anomalies to severe hematologic and organ complications. Diagnosis is often confirmed by chromosomal breakage analysis using DNA cross-linking agents such as diepoxybutane (DEB) or mitomycin C [1].

The global incidence of FA is estimated to be between 1 in 100,000 to 250,000 live births, but rates may be significantly higher in regions with high parental consanguinity, such as the Middle East and parts of South Asia. The heterogeneity of clinical manifestations makes early recognition difficult, especially in resource-limited settings where genetic testing is not always readily available. In such contexts, diagnosis often relies on the presence of suggestive physical anomalies and cytogenetic studies. Early diagnosis is critical to initiate appropriate supportive care, implement surveillance for malignancies, and consider curative treatments like hematopoietic stem cell transplantation (HSCT) [2].

In Egypt, data regarding the clinical spectrum and outcomes of FA are scarce. Understanding the regional characteristics of this disorder can help improve awareness, early diagnosis, and management strategies. Retrospective reviews from specialized centers can provide valuable insights into the disease burden, genotype-phenotype correlations, and long-term outcomes in affected populations.

The aim of this study was to describe the clinical characteristics and outcomes of patients with Fanconi anemia who were followed at a single tertiary care center in Egypt over a 16-year period.

PATIENTS AND METHODS

Study design and setting: This retrospective study was conducted at the Pediatric Hematology Clinic, Ain Shams University Children's Hospital. Medical records of children diagnosed with Fanconi anemia (FA) between January 2005 and December 2021 were reviewed. Data collection was performed over a 12-month period. Of a total of 70 diagnosed patients, 46 medical files were available and included in the final analysis, while 24 files were excluded due to unavailability.

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Inclusion criteria: Confirmed diagnosis of Fanconi anemia based on clinical features suggestive of the condition and evidence of chromosomal breakage on diepoxybutane (DEB) testing. Patients with alternative causes of bone marrow failure, such as dyskeratosis congenita, idiopathic aplastic anemia, or megakaryocytic thrombocytopenia, were excluded from the study.

Data collection and analysis

A comprehensive review of each patient's file was conducted. Extracted data included demographic information (age, sex, consanguinity, and residence), clinical history (age at presentation and diagnosis, presenting features, family history), and physical examination findings. Laboratory investigations included complete blood count (CBC), DEB assay, chromosomal analysis, and bone marrow aspirate/biopsy with evaluation of cellularity and dysplastic changes. Treatment details—such as use of androgens, supportive care (e.g., transfusions), and hematopoietic stem cell transplantation—were recorded. Outcomes assessed included mortality, evidence of myelodysplasia, and progression to acute leukemia.

Ethical considerations: Ethical approval for the study was obtained from the Research Ethics Committee, Faculty of Medicine, Helwan University. Official permission was also granted by Ain Shams University Hospital. Patient confidentiality was strictly maintained by anonymizing all collected data, which were coded and used solely for research purposes. All procedures were conducted strictly in alignment with ethical standards stipulated by the World Medical Association's Declaration of Helsinki governing human research. Written informed consents were obtained from all participants.

Statistical analysis

Data management and statistical evaluation were performed using IBM SPSS Statistics software, version 28 (IBM Corp., Armonk, NY, USA). Categorical variables were reported as frequency counts and percentages.

RESULTS

In this study, we retrospectively reviewed the records of children diagnosed with Fanconi anemia from January 2005 through December 2021 at the Pediatric Hematology Clinic, Ain Shams University Children's Hospital. Among the 46 patients, males predominated (65.2%). Parental consanguinity was high (84.4%), with 43% having a family history of Fanconi anemia and 13.3% a family history of malignancy. Most were Egyptian (95.7%), residing mainly in Greater Cairo and Giza (65.9%). Recurrent infections were reported in 43.5%, with no cases presenting with AML or other malignancies. Common somatic features included microcephaly (58.7%), short stature (55.8%), skin pigmentation (47.8%), and skeletal anomalies (45.6%), while renal/genital (39.5%), ear (27.3%), cardiac (11%), eye (4.3%), and gastrointestinal anomalies (4.3%) were less frequent (Table 1 and figures 1 & 2).

Table (1): Demographic characteristics and clinical signs on examination in the study participants

Variable	N = 46 (No%)
Sex (n=46)	
Male	30 (65.2%)
Female	16 (34.8%)
Parental consanguinity (n=45)	+
Negative	7 (15.6%)
Positive	38 (84.4%)
Family history of FA (n=44)	
Negative	25 (56.8%)
Positive	19 (43%)
Family history of malignancy (n=45)	
Negative	39 (86.7%)
Positive	6 (13.3%)
Nationality (n=46)	
Egyptian	44 (95.7%)
Sudanese	2 (4.3%)
Residence (n=44)	
Great Cairo & Giza	29 (65.9%)
Delta	4 (9.1%)
Canal	3 (7%)
Upper Egypt	8 (18%)
Repeated infections	20 (43.5%)
AML at presentation	0 (0%)
Other malignancies at presentation	0 (%)
Somatic features	
Microcephaly (n=41)	27 (58.7%)
Short stature (n=43)	24 (55.8%)
Skin pigmentation (n=46)	22 (47.8%)
Skeletal anomalies (n=46)	21 (45.6%)
Renal or genital anomalies (n=43)	17 (39.5%)
Ear anomalies (n=44)	12 (27.3%)
Cardiac anomalies (n=45)	5 (11%)
Eye anomalies	2 (4.3%)
Gastrointestinal anomalies	2 (4.3%)
Others*	1 (2.2%)

FA: Fanconi Anemia, AML: Acute Myeloid Leukemia, n:Number, %:Percentage.

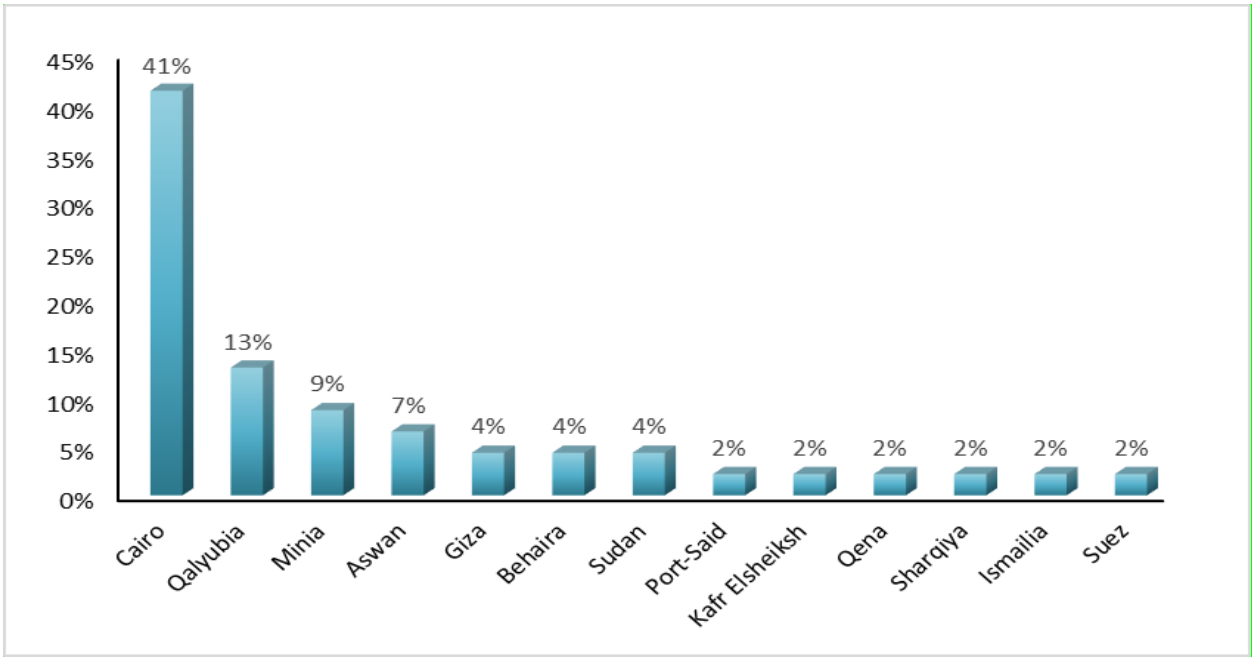

Figure (1): Residence governorate of the study participants.

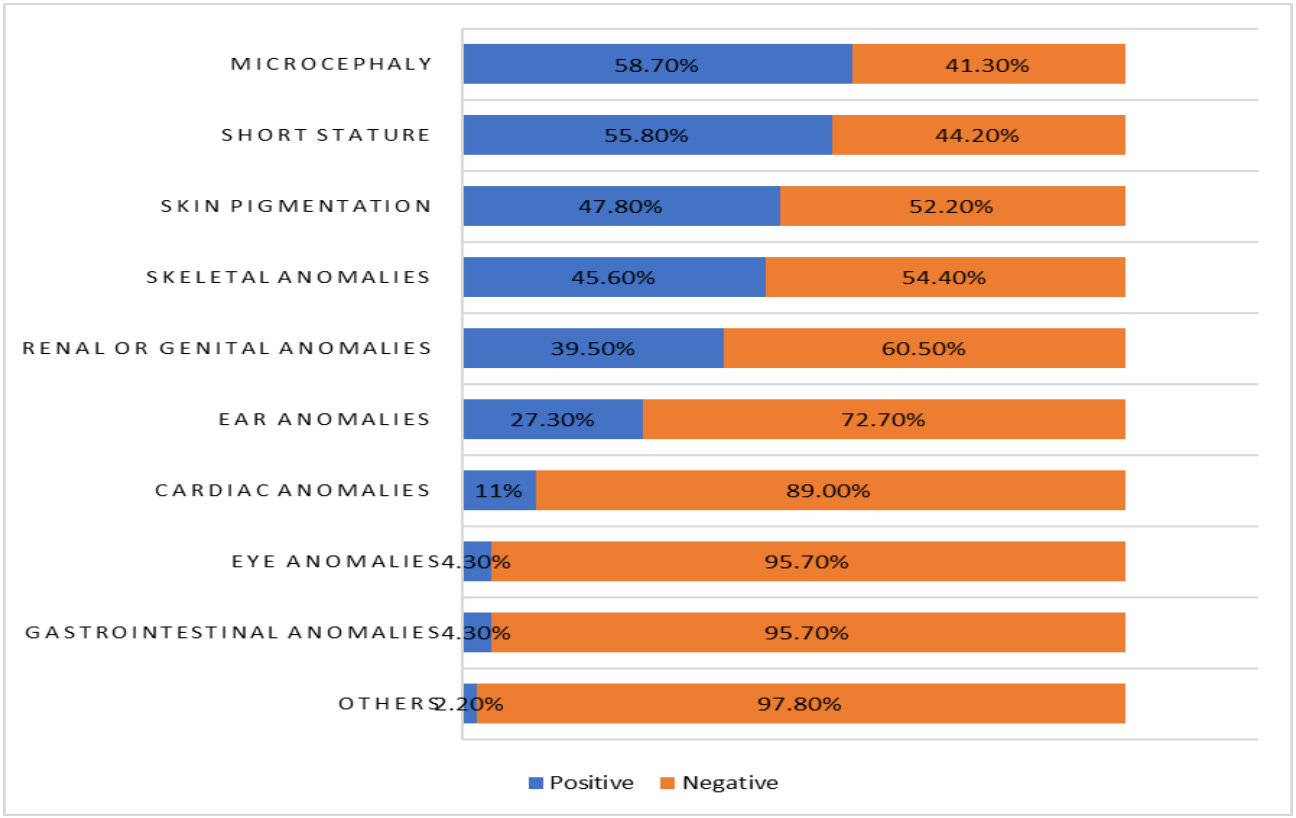

Figure (2): Clinical signs on examination in the study participants.

Microcephaly represented 58.7%, short stature represented 55.8%, skin pigmentation represented 47.8%, skeletal anomalies represented 45.6%, renal anomalies represented 39.5%, and GIT anomalies represented 30%. More than half of the participants (58%) came from Greater Cairo (Cairo, Giza and Qalioubiya), two patients were of African origin (Sudanese) who came for treatment in our country. Among the 42 patients with available bone marrow aspirate/biopsy (BMA/BMB) cellularity data, 95% exhibited hypocellularity, while 5% had normocellular marrow. Dysplastic features were observed in 20.5% of the 44 assessed cases, whereas 79.5% showed no dysplasia. No patients (0%) were diagnosed with acute myeloid leukemia (AML) at presentation. Cytogenetic analysis revealed 1q+ abnormality in 2.2% of cases (Table 2).

Table (2): Bone marrow examination and disease progression in the study participants.

Variable	N = 46 (No%)
BMA/BMB cellularity (n=42) (4 missed)	
Hypocellular	40 (95%)
Normocellular	2 (5%)
Dysplastic features (n=44) (2 missed)	
Present	9 (20.5%)
Absent	35 (79.5%)
AML at diagnosis (n=46)	
Present	0 (0%)
Absent	44 (100%)
Cytogenetics (n=46)	
1q+	1 (2.2%)

BMA: Bone Marrow Aspirate, BMB: Bone Marrow Biopsy, AML: Acute Myeloid Leukemia, n: Number, %: Percentage.

DISCUSSION

This retrospective study described the clinical features and outcomes of young Egyptian patients with Fanconi anemia. The study provided valuable insights into the characteristics of such a rare condition, available management options and disease outcomes in a resource-limited setting. Fanconi anemia is an autosomal recessive bone marrow failure syndrome, more common in regions with high consanguinity and large family sizes, such as the Middle East. **Khayat and Saxena** [3] reported higher rates in rural than urban areas and in Upper Egypt compared to Lower Egypt. In this study, parental consanguinity was frequent, with nearly half of the patients having a family history of Fanconi anemia, highlighting the need for preventive strategies and antenatal testing in high-risk populations.

Kesici *et al.* [4] reported parental consanguinity in most Turkish patients, similar to our findings. In contrast, **Al-Sabbagh *et al.*** [5] found a lower rate in Saudi patients with FA suggesting a higher carrier rate in Saudi Arabia. FA is characterized by a gradual failure of the bone marrow, with consequent hematological abnormalities and an increased susceptibility to infections. In the current study, a large majority of the patients presented with hematological abnormalities with anemia being more common than thrombocytopenia and almost half of the patients suffered from recurrent infections. These findings refer to the importance of early detection and management of hematologic abnormalities in patients with Fanconi anemia [6]. Regular monitoring of blood counts and appropriate interventions, such as blood transfusions and hematopoietic stem cell transplantation when indicated, are crucial in optimizing patient outcomes.

FA is a rare genetic disorder caused by DNA repair defects in multiple genes. Diagnosis relies on somatic features, bone marrow failure, chromosomal breakage assays with DEB or mitomycin, and genetic testing. In this study, DEB assay was the primary diagnostic tool with most patients showing high breakage induction. One patient diagnosed through genetic testing, lacked typical somatic features but had persistent isolated neutropenia. A major challenge in the chromosome breakage assay is mosaicism. In FA, somatic mosaicism results from reversion or compensatory mutations in HSPCs, leading to a mix of blood cells with and without functional DNA repair. Patients often exhibit two distinct cell populations: One sensitive to DNA-damaging agents, confirming FA [7].

The diverse presentation of FA is linked to the relationship between clinical features and genetic causes. Early diagnosis and identification of patient-specific pathogenic variants are crucial for guiding clinical management, particularly in severe cases [8].

This single-center study with a small sample size lacked genetic testing for all patients and did not assess age or treatment effects on survival. Variations in treatment modalities may have influenced outcomes.

CONCLUSION

This study highlighted the clinical burden of Fanconi anemia among Egyptian children, emphasizing the high rates of parental consanguinity, congenital anomalies, and bone marrow failure. The absence of leukemia at presentation and the predominance of hypocellular marrow underscored the progressive nature of the disease. Early diagnosis through chromosomal breakage testing, along with comprehensive supportive care and timely referral for stem cell transplantation, remains crucial. These findings underscored the need for increased awareness, genetic counselling, and improved access to specialized care in resource-limited settings.

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Conflict of Interest: Nil.

REFERENCES

1. **Park M (2022)**: Overview of inherited bone marrow failure syndromes. Blood Res., 57: 49-54.
2. **Bhandari J, Thada P, Killeen R *et al.* (2024)**: Fanconi anemia: StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559133/.
3. **Khayat G, Saxena C (2004):** eConsanguinity and its effect on infant and child mortality in Egypt. Available at https://ipc2005.popconf.org/abstracts/50388.
4. **Kesici S, Ünal Ş, Kuşkonmaz B *et al.* (2019)**: Fanconi anemia: a single center experience of a large cohort. Turk J Pediatr., 61: 477-84.
5. **Al-Sabbagh A, Alzahrani H, Dasouki J *et al.* (2022)**: Clinical Characterization, Cancer Incidence and Long-Term Outcomes of Fanconi Anemia Patients : A Single Center Analysis of 97 Patients. Blood, 140: 11471-3.
6. **Dufour C, Pierri F (2022)**: Modern management of Fanconi anemia. Hematology Am Soc Hematol Educ Program, 2022(1):649-657.
7. **Merfort W, Lisboa O, Cavalli R *et al.* (2022)**: Cytogenetics in Fanconi Anemia: The Importance of Follow-Up and the Search for New Biomarkers of Genomic Instability. Int J Mol Sci., 23: 14119.
8. **Velleuer E, Dietrich R, Pomjanski N *et al.* (2020)**: Diagnostic accuracy of brush biopsy-based cytology for the early detection of oral cancer and precursors in Fanconi anemia. Cancer Cytopathol., 128: 403-13.