Original Article

Hematological malignancies

Prevalence and hematological characteristics in a single center in southern Saudi Arabia

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ABSTRACT

الأهداف: تهدف الدراسة إلى تحديد مدى انتشار سرطان الدم في منطقة عسير بالمملكة العربية السعودية وتوضيح أهمية النتائج المخبرية في الدم والكيمياء الحيوية والتخثر لمرضى سرطان الدم في سياق إدارة المرض.

المنهجية: شملت هذه الدراسة 210 مريضًا بين عامي 2012 و2022. حيث تم تشخيص إصابتهم بسرطان الدم في أعمار مختلفة. تم استخدام اختبار T المتعدد غير المقترن لمقارنة مرضى سرطان الدم مع عينات المراقبة، والتي تتألف من أشخاص أصحاء، وتم اعتبار قيمة عند $p<0.05$ كقيمة مهمة. تم تجميع البيانات من مستشفى عسير المركزي بمنطقة عسير، وتم جمعها من خلال مسحة الدم المحيطية وخزعة النخاع العظمي (2012–2017) أو عن طريق قياس التدفق الخلوي (2018–2022)، وفقًا لنظام المعلومات الصحية الخاص بالمستشفى وسجل البيانات لدى المرضى.

النتائج: من إجمالي 210 مريض بسرطان الدم (61% ذكور و39% إناث)، تم تشخيص 104 حالات (2012–2017) بناء على مسحة الدم المحيطية وخزعة نخاع العظم، و106 حالات (2018–2022) وعلى أساس قياس التدفق الخلوي. تم تحديد خمسة عشر نوعًا فرعيًا من سرطان الدم، وكان سرطان الدم النخاعي المُزمن هو الأكثر شيوعًا (34.2%)، يليه سرطان الدم النخاعي الحاد (17.6%)، وسرطان الدم الليمفاوي المزمن (11.9%)، وسرطان الدم الليمفاوي الحاد في الخلايا البائية (9.5%). بالإضافة على حالات نادرة أخرى.

الخلاصة: من بين 210 حالات سرطان الدم التي تم تشخيصها في منطقة عسير بالمملكة العربية السعودية بين عامي 2012–2022، كان النوع الفرعي الأكثر شيوعًا هو سرطان الدم النخاعي المزمن، يليه سرطان الدم النخاعي الحاد. في جميع أنواع سرطان الدم الفرعية، لوحظت تغييرات كبيرة مميزة في معايير الدم، والعوامل البيوكيميائية، وملامح التخثر.

Objectives: To determine the prevalence of leukemia in the Aseer region of Saudi Arabia and the importance of hematological, biochemical and coagulation profiles for leukemic patients in the context of disease management.

Methods: This retrospective study comprised 210 patients between 2012 and 2022 who had been diagnosed with leukemia at different ages. The multiple unpaired t-test was used to compare leukemic patients with control samples,which consisted of healthy individuals, and $p<0.05$ was taken as significant. The data was compiled from Aseer Central Hospital in the Aseer region and collected through peripheral blood smear and bone marrow biopsy (2012-2017) or by flow cytometry (2018-2022), according to the hospital information system and registry data.

Results: Of the total 210 leukemic patients (61.4% males and 38.6% females), 104 cases (2012-2017) were diagnosed based on peripheral blood smear and bone marrow biopsy,and 106 cases (2018-2022) based on flow cytometry. Fifteen subtypes of leukemia were identified, with chronic myeloid leukemia being the most common (34.2%), followed by acute myeloid leukemia (17.6%), chronic lymphoblastic leukemia (11.9%), and B-cell acute lymphoid leukemia (9.5%). Other rare cases were also found.

Conclusion: Of the 210 leukemia cases diagnosed in the Aseer region between 2012-2022, the most common subtype was chronic myeloid leukemia, followed by acute myeloid leukemia. In all leukemia subtypes, distinctive significant changes were observed in hematological parameters, biochemical parameters, and coagulation profiles.

Keywords: hematological malignancies, prevalence, laboratory findings

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Leukemia in general is a highly prevalent malignant condition that affects individuals worldwide.[1] The etiology of leukemia has yet to be fully elucidated, although it is believed to stem from a variety of factors including genetic predisposition, environmental influences, radiation exposure, infectious agents, and more besides.[2] In recent years, the incidence of leukemia has exhibited a gradual rise on a global scale, with diagnosed cases increasing from 354,500 to 437,033 between 1990 and 2018, and approximately 309,000 fatalities reported in that period, as per the data published by GLOBOCAN (Global Cancer Statistics) in 2018.[3] Global Cancer Statistics also reported a further increase in leukemia incidence to 474,519 in the year 2020, representing a percentage increase of approximately 2.4%. This places leukemia as the 13 most prevalent cancer type worldwide.[4]

The incidence of leukemia in Saudi Arabia likewise exhibited an upward trend over the period of 1999 to 2013, with a total of 8,712 cases reported for both genders. According to the data from the Saudi Cancer Registry (SCR), the majority of patients diagnosed with leukemia were male (57.2%), with 42.8% being female. Precursor B-cell lymphoblastic leukemia (B-ALL) was found to be the most frequently diagnosed type, accounting for 18.7% of cases.[5] In the year 2018, a total of 799 cases were recorded, comprising 466 male cases and 333 female cases. Meanwhile, in 2020, a total of 1,676 cases were documented, with mortality in 1,032 cases. Collectively, over the past 5 years, the total count was 5,726 cases, including both genders.[3]

It is widely recognized that timely identification and diagnosis of leukemia can result in prompt intervention and thereby enhance patient survival.[6] A standard diagnostic approach involves conducting a physical examination and obtaining a comprehensive family history. Additionally, manual diagnostic methods such as complete blood count (CBC), peripheral blood smear examination via microscope, bone marrow biopsy, flow cytometry, immunohistochemistry, immunophenotyping, gene expression analysis, and x-ray imaging are commonly employed to determine the specific type of white blood cells involved.[7] The compilation of such data across investigations and the utilization of contemporary methodologies in conjunction with conventional techniques contribute substantially to the expeditious advancement of leukemia diagnosis and prognosis, enhancing diagnostic precision and disease detection.[7,8] Importantly, the increasing incidence of leukemia is associated with high mortality due to delayed diagnosis. Computer-aided diagnostic (CAD) systems have been instrumental in overcoming the constraints associated with manual leukemia identification, applying a set of interconnected algorithms that analyze various blood component characteristics, including cell attributes such as shape, color, and size, as well as cytoplasmic features and other factors, to facilitate precise and reliable leukemia diagnosis.[7,8] This automation of disease identification helps facilitate early detection and hence mitigates mortalities.[9]

In general, laboratory analyses play a significant role in identifying noteworthy alterations in parameters and so facilitating the monitoring, prediction, and treatment of patients with leukemia. The observation of changes in parameters is instrumental in achieving a state of health equilibrium and generating prognostic insights for patients.[10]

The objective of this study is to assess the frequency of leukemia cases in the Aseer region of Saudi Arabia from 2012 to 2022. Additionally, it seeks to explore the influence of hematological malignancies on various laboratory indicators, such as hematological, biomedical, and coagulation profiles. The selection of the particular parameters under investigation was predicated upon prior findings indicating substantial alterations, whether in an upward or downward direction, in persons with leukemia as compared to unaffected control subjects.

Methods. This study was carried out in the Aseer Central Hospital (ACH) in the Aseer region located in the south of Saudi Arabia. The data was collected in December 2022 and consisted of 210 leukemic patients, aged 2 to 89 years, seen in the last 10 years (from 2012 to 2022). As per the latest local policy of the hospital, patients who are 15 years of age or older are categorized as adults, whereas children under the age of 14 are classified as pediatrics. This protocol was adhered to throughout the research. Records were taken from the hospital information system (HIS) and register data of ACH. For the 104 cases from 2012 to 2017, data including diagnosis, year, age, and gender were collected from registered data based on peripheral blood smear and bone marrow. For the 106 cases from 2018 to 2022, flow cytometry data was obtained from the HIS and contained diagnosis, year, age, and gender; the CBC parameters white blood cell (WBC), red blood

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cell (RBC), hemoglobin (HB), hematocrit (HTC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), and platelet count; the coagulation parameters prothrombin time (PT), activated partial thromboplastin (APTT), and international normalized ratio (INR), and the liver and renal function biochemistry parameters urea, creatinine, aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), total protein, albumin, direct and total bilirubin. Biochemical parameters of the patients' liver and renal function, in addition to coagulation and CBC parameters, were extracted and analyzed prior to treatment initiation. Patients were excluded if they had any chronic disease, diabetic mellitus, history of liver and kidney disorder, or history of drug use that may affect hematological, coagulation, or liver and kidney function tests. The research ethics committee at King Khalid University (HAPO-06-B-001) granted ethical approval (Approval No: ECM#2023-2128), and the study was carried out in accordance with the Helsinki Declaration principles.

A random set of 100 healthy controls with ages ranging 13 to 91 years (mean 41.08 years) were collected from the laboratory staff and Donation Center. These samples were analyzed using a Sysmex XN-2000TM (Sysmex Corporation, Kobe, Japan) in the hematological laboratory, a Cobas 6000 and Autoanalyzer in the biochemistry laboratory, and a SIEMENS for coagulation tests in the laboratory of ACH.

Statistical analysis. The programs GraphPad Prism (version 9.5.1) (733) and Microsoft Excel 16 were used for analysis. The multiple unpaired t-test was used to compare leukemic patients with the control samples to assess statistically significant differences between the 2 groups, and a *p*-value of <0.05 was taken as significant.

Results. Of the 210 leukemic cases seen in the recent 10 years at ACH, 129 (61.4%) were males and 81 (38.6%) were females. The mean age was 44.13 ± 24.71. These patients represented all 4 main types of leukemia: chronic myeloid leukemia (CML), acute myeloid leukemia (AML), acute lymphoid leukemia (ALL), and chronic lymphoid leukemia (CLL). The controls consisted of 100 healthy persons, including males and females of different ages. Table 1 displays the distribution of leukemia cases among children aged 14 years or younger, categorized by gender, type, and subtype, spanning from 2012 to 2022. The prevailing type was acute lymphoblastic leukemia (ALL), accounting for 10 cases (30.3%). Chronic myeloid leukemia and ALL-L2 were the second most prevalent, accounting for 5 cases (15.1%). Acute myeloid leukemia, CLL, ALL-L3, and AML-M4 accounted for 2 cases, or 6% of the total. AML-M3, ALL-L1, AML-M2, AML-M7, and AML-M1 had the lowest occurrence, with only 1 case each, accounting for 3% of the total cases. Table 2 illustrates the distribution of leukemia cases among adults aged 15 years or older, categorized by gender, type, and subtype, covering the period from 2012 to 2022. With 67 (37.8%) cases, CML was the most prevalent, followed by AML with 35 (19.7%) cases. Chronic lymphoid leukemia ranked third with

Table 1 - Distribution of leukemia cases by gender, type, and subtype among children aged 14 years or younger from 2012 to 2022.

Leukemia subtype	Male	Female	Total
ALL	7 (70)	3 (30)	10 (30.3)
CML	5 (100)	0 (0)	5 (15.1)
ALL-L2	4 (80)	1 (20)	5 (15.1)
AML	0 (0)	2 (100)	2 (6)
CLL	2 (100)	0 (0)	2 (6)
ALL-L3	2 (100)	0 (0)	2 (6)
AML-M4	0 (0)	2 (100)	2 (6)
AML-M3	1 (100)	0 (0)	1 (3)
ALL-L1	1 (100)	0 (0)	1 (3)
AML-M2	1 (100)	0 (0)	1 (3)
AML-M7	1 (100)	0 (0)	1 (3)
AML-M1	1 (100)	0 (0)	1 (3)
TOTAL	25 (75.7)	8 (24.2)	33 (100)

Values are presented as numbers and percentages (%). ALL: acute lymphoid leukemia, CML: chronic myeloid leukemia, AML: acute myeloid leukemia

Table 2 - Distribution of leukemia cases by gender, type, and subtype among adults aged 15 years or older from 2012 to 2022.

Leukemia subtype	Male	Female	Total
CML	43 (64.1)	24 (35.8)	67 (37.8)
AML	23 (65.7)	12 (34.2)	35 (19.7)
CLL	10 (43.4)	13 (56.5)	23 (12.9)
B-ALL	9 (45.0)	11 (55.0)	20 (11.2)
ALL	6 (66.6)	3 (33.3)	9 (5)
ALL-L2	5 (62.5)	3 (37.5)	8 (4.5)
AML-M3	2 (40)	3 (60)	5 (2.8)
T-ALL	1 (33.3)	2 (66.7)	3 (1.6)
ALL-L3	1 (50)	1 (50)	2 (1.2)
AML-M4	0	1 (100)	1 (0.5)
ALL-L1	1 (100)	0	1 (0.5)
AML-M2	1 (100)	0	1 (0.5)
AML-M7	1 (100)	0	1 (0.5)
AML-M5	1 (100)	0	1 (0.5)
TOTAL	104 (58.7)	73 (41.2)	177 (100)

Values are presented as numbers and percentages (%). ALL: acute lymphoid leukemia, CML: chronic myeloid leukemia, AML: acute myeloid leukemia

23 (12.9%) cases, followed by B-ALL with 20 (11.2%) cases. ALL represents 9 (5%) cases, whereas ALL-L2 represents 8 (4.5%) cases. The following conditions occurred before the last: AML-M3 (2.8%), T-ALL (1.6%), and ALL-L3 (1.2%). AML-M4, ALL-L1, AML-M2, AML-M7, and AML-M5 each accounted for one (0.5%) case at the end.

In CML patients, WBC count was significantly increased (mean=242.3, SEM=16.76) with $p<0.001$, as was platelet count (mean=354.5, SEM=24.46) with $p=0.02$. The HB level in patients was significantly decreased (mean=10.72, SEM=0.4132) with $p<0.001$, along with both RBC count (mean=3.859, SEM=0.1675) with $p<0.001$ and HCT (mean=33.11, SEM=1.228) with $p<0.001$. In contrast, RDW ratio (mean=19.48, SEM=0.3524) was significantly increased with $p<0.001$ (**Figure 1A**).

In AML patients, a significant increase was evident in WBC count (mean=50.52, SEM=7.448) with $p<0.001$. This was accompanied by a significant decrease in platelet count (mean=57.90, SEM=15.39) with $p<0.001$. We further found decreases in HB level (mean=8.339, SEM=0.3580) with $p<0.001$, in RBC count (mean=2.842, SEM=0.1364) with $p<0.001$,

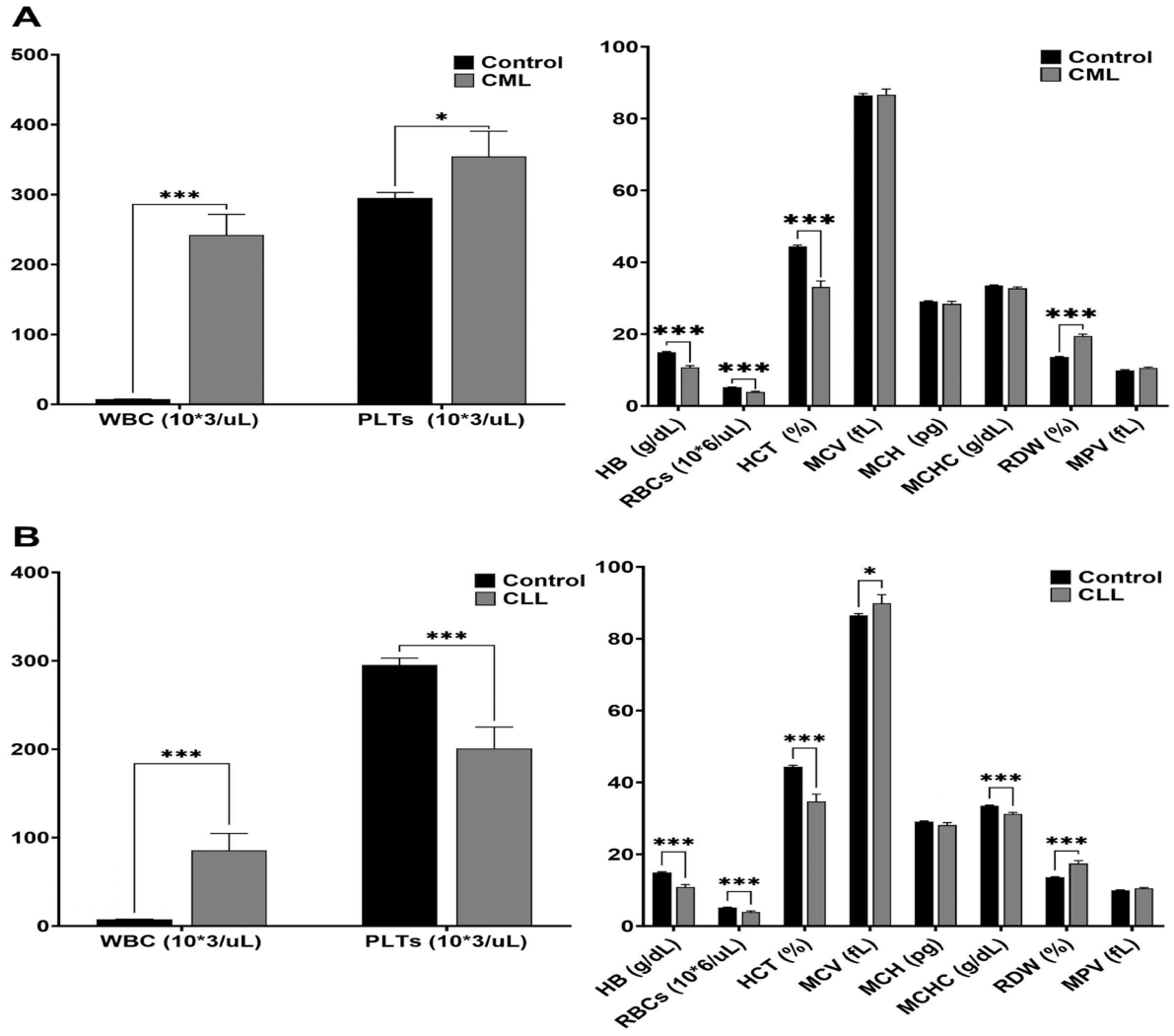

Figure 1 - Comparison of CBC parameters between patients with (**A**) chronic myeloid leukemia (CML) and (**B**) chronic lymphoid leukemia (CLL) and control groups. The total sample comprised 106 leukemic patients and 100 controls. Evaluated parameters include white blood cells (WBC), platelets (PLTs), hemoglobin (HB), red blood cells (RBCs), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), and mean platelet volume (MPV). *$p<0.05$, ***$p<0.001$

and in HCT (mean=25.28, SEM=0.9813) with $p<0.001$. In contrast, MCV was significantly increased (mean=89.83, SEM=1.378) with $p=0.02$. Finally, the RDW ratio was significantly increased (mean=17.98, SEM=0.3657) with $p<0.001$ (**Figure 2A**).

In CLL patients, we observed a significant increase in WBC count (mean=85.81, SEM=8.557) with $p<0.001$. Conversely, significant decreases were demonstrated in platelet count (mean=201, SEM=20.12) with $p<0.001$, HB level (mean=10.88, SEM=0.4898) with $p<0.001$, and RBC count (mean=3.936, SEM=0.1820) with $p<0.001$. The HCT ratio also showed a significant decrease (mean=34.71, SEM=1.324) with $p<0.001$. Meanwhile, MCV was significantly increased (mean=89.89, SEM=1.547) with $p=0.03$, but MCHC was significantly decreased (mean=31.21, SEM=0.4482) with $p<0.001$. Finally, the RDW ratio was significantly increased (mean=17.41, SEM=0.4348) with $p<0.001$ (**Figure 1B**).

In B-cell ALL, patients showed a significant increase in WBC count (mean=88.66, SEM=13.69) with $p<0.001$. Conversely, significant decreases were observed in platelet count (mean=40.45, SEM=18.09) with $p<0.001$, HB level (mean=9.330, SEM=0.4806) with $p<0.001$, RBC count (mean=3.355, SEM=0.1768) with $p<0.001$, and HCT (mean=29.30, SEM=1.333) with $p<0.001$. Also significantly decreased were MCH (mean=27.37, SEM=0.4743) with $p<0.001$ and MCHC (mean=31.54, SEM=0.4770) with $p<0.001$, while RDW ratio was significantly increased (mean=17.36, SEM=0.4030) with $p<0.001$ (**Figure 2B**).

In T-ALL patients, we observed a significant increase in WBC count (mean=32.43, SEM=3.117) with $p<0.001$. In contrast, significant decreases were seen in platelet count (mean=119.7, SEM=44.94) with $p<0.001$, HB level (mean=9, SEM=1.011) with $p<0.001$, RBC count (mean=3.27, SEM=0.3741) with $p<0.001$, HCT (mean=28.60, SEM=2.581) with $p<0.001$, and MCHC (mean=31.23, SEM=1.092) with $p=0.04$. Meanwhile, RDW ratio was significantly increased (mean=24.10, SEM=0.8632) with $p<0.001$ (**Figure 2C**).

Chronic myeloid leukemia patients exhibited significantly increased total bilirubin (mean=0.5629, SEM=0.04733) with p-value 0.006, as well as significant increases in both AST (mean=29, SEM=1.599) with $p<0.001$ and ALP (mean=97.52, SEM=6.896) with p-value 0.008. Meanwhile, albumin was significantly decreased (mean=3.936, SEM=0.1132) with $p<0.001$, but GGT also significantly increased (mean=53.13, SEM=4.345) with $p<0.001$ (**Figure 3A**).

Acute myeloid leukemia patients exhibited significant increases in nearly all examined biochemistry parameters, including total bilirubin (mean=0.8881, SEM=0.08712) with $p<0.001$, direct bilirubin (mean=0.3931, SEM=0.07716) with $p=0.006$, urea (mean=51.29, SEM=5.274) with $p<0.001$, ALT (mean=32.12, SEM=4.006) with $p=0.001$, AST (mean=88.09, SEM=31.13) with $p=0.04$,and ALP (mean=99, SEM=8.954) with $p=0.03$. Total protein was significantly decreased (mean=6.863, SEM=0.1418) with $p<0.001$, as was albumin (mean=3.308, SEM=0.1199) with $p<0.001$, while GGT was significantly increased (mean=62.42, SEM=8.006) with $p<0.001$ (**Figure 4A**).

CLL patients likewise exhibited significant increases in most biochemistry parameters, including: creatinine (mean=1.277, SEM=0.09933) with $p=0.03$, total bilirubin (mean=0.6692, SEM=0.06055) with $p<0.001$, direct bilirubin (mean=0.2533, SEM=0.03160) with $p=0.02$, urea (mean=67.99, SEM=9.537) with $p<0.001$, ALT (mean=29.69, SEM=4.179) with $p=0.02$, AST (mean=32.97, SEM=4.423) with $p=0.02$, and ALP (mean=96.88, SEM=6.970) with $p=0.01$. Total protein in these patients was significantly decreased (mean=6.796, SEM=0.1548) with $p<0.001$, as was albumin (mean=3.862, SEM=0.1506) with $p<0.001$, whereas GGT was significantly increased (mean=38.60, SEM=4.915) with $p=0.004$ (**Figure 3B**).

In B-ALL patients, all biochemistry parameters were significantly altered except total protein. The altered parameters were as follows: increased creatinine (mean=1.093, SEM=0.05518) with $p=0.03$, total bilirubin (mean=1.272, SEM=0.1931) with $p<0.001$, direct bilirubin (mean=0.7276, SEM=0.1767) with $p=0.002$, urea (mean=39.28, SEM=2.887) with $p<0.001$, ALT (mean=79.99, SEM=12.30) with $p<0.001$, AST (mean=60.23, SEM=6.142) with $p<0.001$, and ALP (mean=128.8, SEM=9.973) with $p<0.001$; decreased albumin (mean=3.718, SEM=0.1252) with $p<0.001$; and increased GGT (mean=180.2, SEM=23.22) with $p<0.001$ (**Figure 4B**).

In T-ALL patients, most biochemistry parameters were not significantly altered; the exceptions were creatinine, which was significantly decreased (mean=0.7000, SEM=0.05580) with $p<0.001$, and albumin, which was significantly decreased (mean=3.40, SEM=0.2854) with $p<0.001$ (**Figure 4C**).

The coagulation profiles of CML patients showed significant increase in PT (mean=14.56, SEM=0.3567) with $p<0.001$, APPT (mean=35.61, SEM=0.9589) with $p<0.001$, and also INR (mean=1.266, SEM=0.03103) with $p<0.001$. AML patients similarly showed a

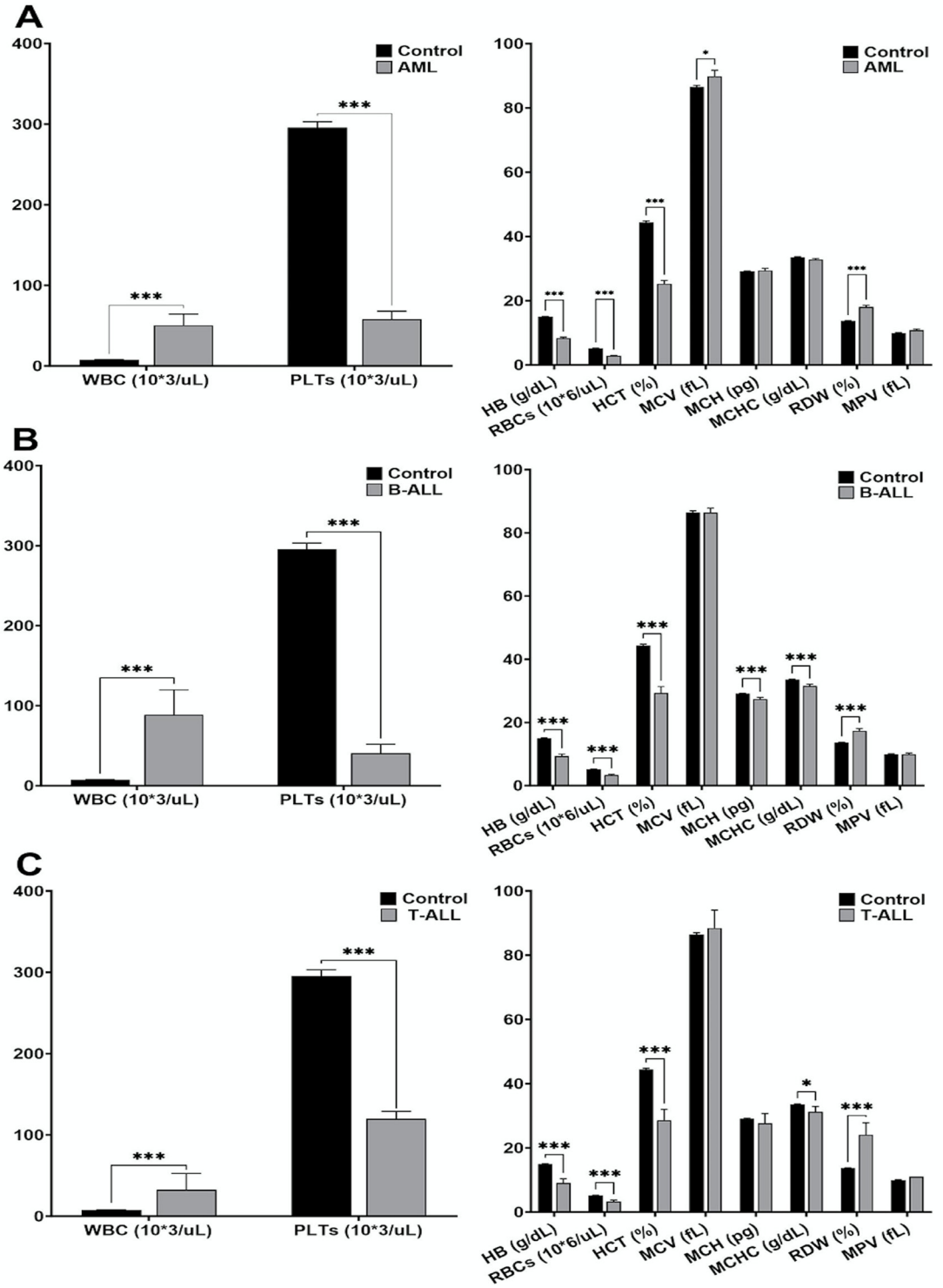

Figure 2 - Comparison of CBC parameters between patients with (**A**) acute myeloid leukemia (AML), (**B**) B-cell acute lymphoid leukemia (B-ALL), and (**C**) T-cell acute lymphoid leukemia (T-ALL) and control groups. The total sample included 106 leukemic patients with 100 controls. Evaluated parameters include white blood cells (WBC), platelets (PLTs), hemoglobin (HB), red blood cells (RBCs), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), and mean platelet volume (MPV).*p<0.05, ***p<0.001.

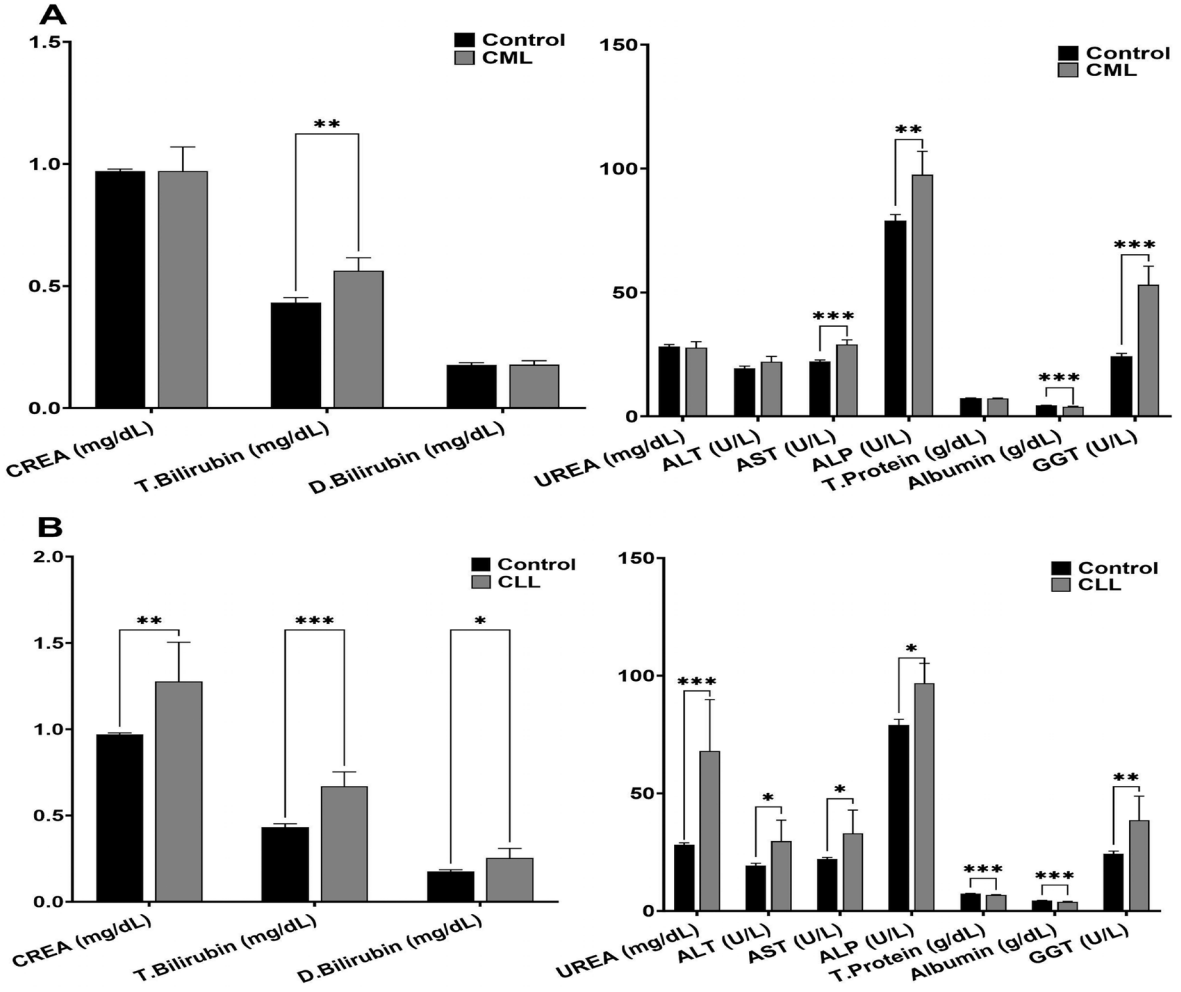

Figure 3 - Comparison of liver and kidney function tests between patients with (**A**) chronic myeloid leukemia (CML) and (**B**) chronic lymphoid leukemia (CLL) and control groups. The total sample includes 106 leukemic patients with 100 controls. Evaluated parameters include creatinine (CREA), total bilirubin (T. Bilirubin), direct bilirubin (D. Bilirubin), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total protein (T. Protein), and gamma-glutamyl transferase (GGT). *p<0.05, **p<0.01, ***p<0.001.

significant increase of PT (mean=14.61, SEM=0.4480) with p<0.001 and also of INR (mean=1.270, SEM=0.03889) with p<0.001. The coagulation profiles of CLL patients exhibited no significant difference in any parameter. Likewise, B-ALL patients did not show any significant alteration of coagulation profiles. Finally, T-ALL patients also did not show significant change in coagulation profiles (Figure 5).

Discussion. Leukemia is a malignancy distinguished by the presence of aberrant cells within the hematopoietic system, specifically in the blood and bone marrow. According to the GLOBOCAN database, leukemia ranked as the 13th most prevalent disease worldwide in 2018. Additionally, there was a notable 17% rise in leukemia-related deaths during same year.[11] According to the Saudi Cancer Registry (SCR), there has been a notable rise in the incidence of leukemia cases within the local context of Saudi Arabia.[5] The aforementioned rise persists, notwithstanding current advancements in detection and therapeutic interventions for individuals with leukemia.[12] The present investigation centers on examining the frequency of the predominant subtypes of leukemia in the Aseer region of Saudi Arabia during the period spanning from 2012 to 2022. Additionally, it aims to explore the association between leukemia and various laboratory parameters, specifically hematological parameters, biochemical parameters, and coagulation profiles.

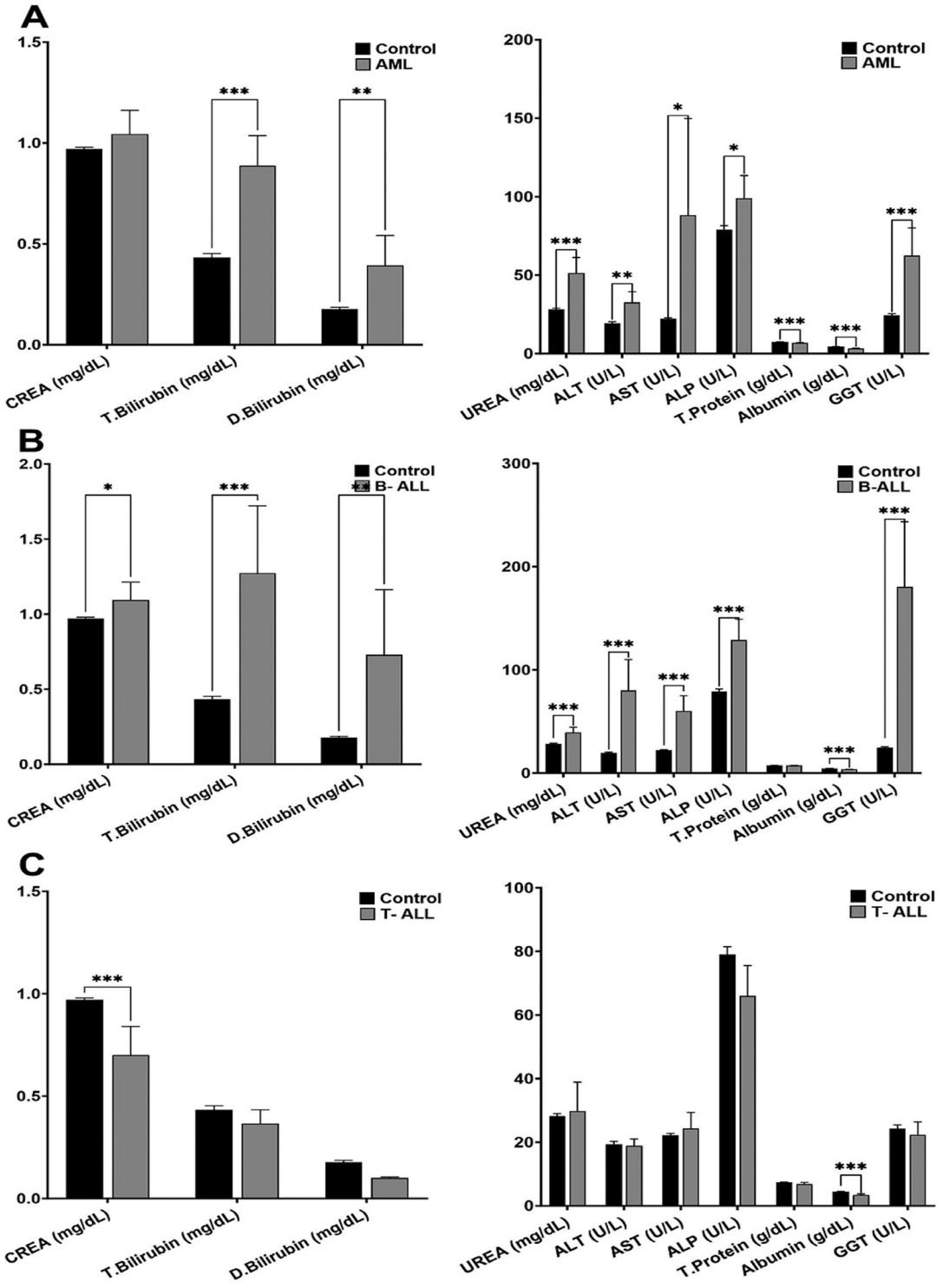

Figure 4 - Comparison of liver and kidney function tests between patients with (**A**) acute myeloid leukemia (AML), (**B**) B-cell acute lymphoid leukemia (B-ALL), and (**C**) T-cell acute lymphoid leukemia (T-ALL) and control groups. The total sample includes 106 leukemic patients with 100 controls. Evaluated parameters include creatinine (CREA), total bilirubin (T. Bilirubin), direct bilirubin (D. Bilirubin), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total protein (T. Protein), and gamma-glutamyl transferase (GGT). *p<0.05, **p<0.01, ***p<0.001.

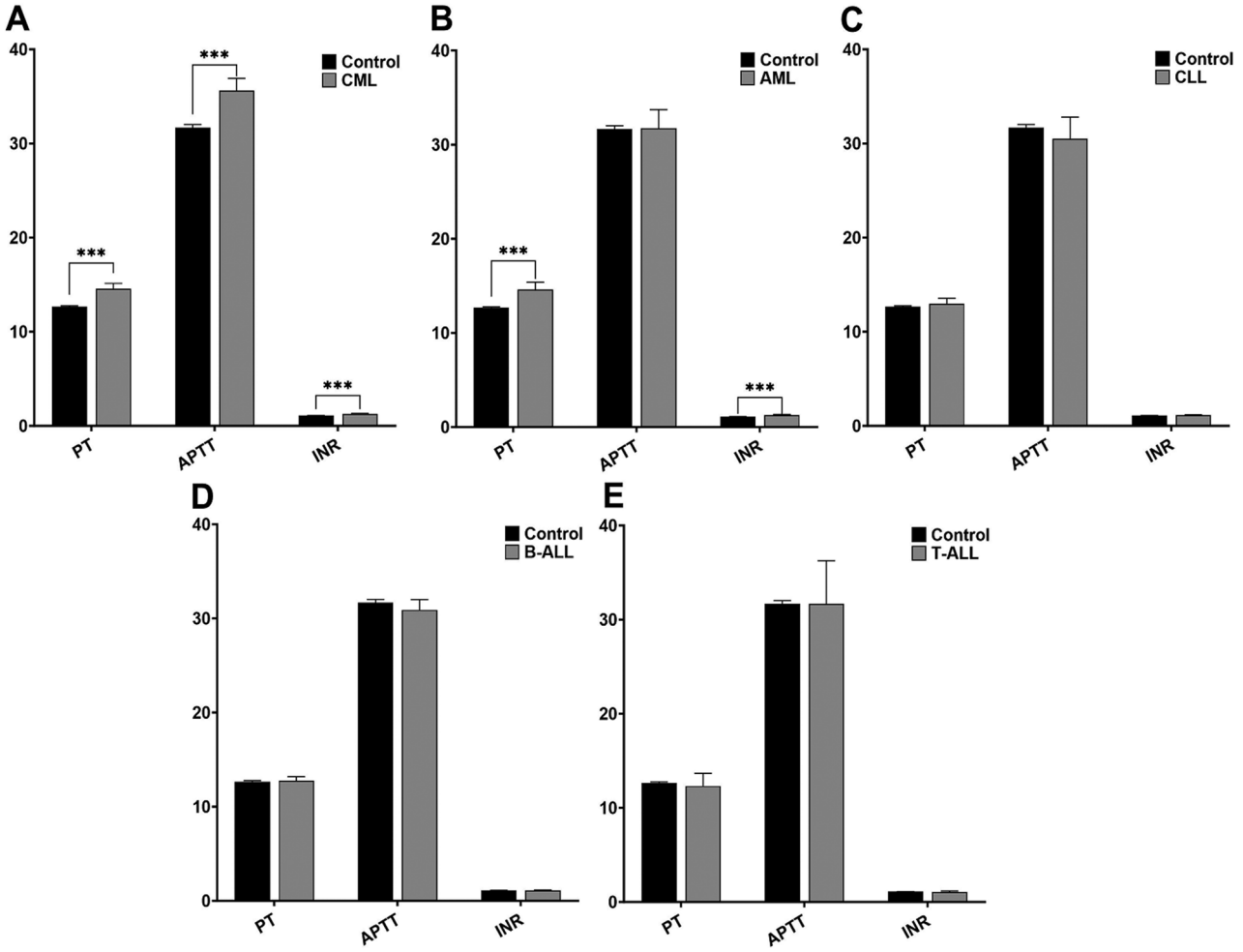

Figure 5 - Comparison of coagulation profiles between patients with (**A**) chronic myeloid leukemia (CML), (**B**) acute myeloid leukemia (AML), (**C**) chronic lymphoid leukemia (CLL), (**D**) B-cell acute lymphoid leukemia(B-ALL), and (**E**) T-cell acute lymphoid leukemia (T-ALL) and control groups. The total sample includes 106 leukemic patients with 100 controls. Sig: ***p<0.001. PT: prothrombin time, APTT: activated partial thromboplastin, INR: international normalized ratio

In the Aseer Central Hospital, located in the Aseer region of Saudi Arabia, a total of 210 patients were diagnosed with leukemia over the past decade. Among these patients, there were more males (129, 61.4%) than females (81, 38.6%).This distribution is consistent with a previous study carried out in the Aseer region of Saudi Arabia between 1999–2013, which documented 1254 cases, of which a majority were male (705, 56.2% versus 549, 43.77%).[5]

Chronic myeloid leukemia is a myeloproliferative neoplasm which affects 1-2 individuals out of every 100,000. It is caused by genetic changes, particularly the presence of the Ph chromosome in the bone marrow cells and the translocation t (9;22) (q34; q11.2), which includes the including abnormal BCR-ABL1 gene.[13] The progression of CML is triphasic, consisting of a chronic phase, an accelerated phase, and a blast phase. Cases are mostly diagnosed in the chronic phase, which converts to a blast crisis (acute phase) if there is no medical intervention.[14]

At the global scale, CML cases grew from 31.8 thousand in 1990 to 34.2 thousand in 2017, despite being considered rarely diagnosed compared to the other main types of leukemia (ALL, AML, CLL).[15] Our research findings indicate that CML is the predominant form of leukemia among all 210 patients, represented by 72 (34.2%) cases, of which 47 (65.3%) were male and 25 (34.7%) female, when considering all age groups.In contrast, a previous study in Saudi Arabia identified chronic myeloid leukemia as the third ranking

diagnosed type during 1999-2013, at 1131 (13%) of 8712 cases.[5] The high prevalence of CML in the Aseer region may be due to genetic reasons, environmental causes, or exposure to radiation and chemotherapy.[14] The latest findings of recent studies on the treatment of chronic phase CML recommend the use of tyrosine kinase inhibitors (TKIs) for those newly diagnosed.[13]

Acute myeloid leukemia is primarily an adult cancer that starts from the bone marrow, spreads to the blood, and then sometimes spreads to other organs such as the liver and spleen.[16] Acute myeloid leukemia is characterized by the proliferation of myeloid blasts to the point of accounting for ≥20% of cells in blood and bone marrow, and according to the French-American-British classification is categorized into types M0 through M7 based on morphology and cytochemistry. Although important advances in our knowledge of its molecular pathophysiology have resulted in advancements in diagnosis, monitoring, and treatment, AML remains a difficult illness to treat.[17]

Among the 210 cases examined in our study, AML (not specific) was found to be the second most prevalent kind of leukemia, accounting for 37 (17.6%) cases. In a previous study in 2018, AML likewise ranked as the second most common type in Saudi Arabia.[3] The reasons for high AML prevalence may include hereditary factors and also lifestyle factors such as smoking, chemicals, and radiation.[16]

Chronic lymphoid leukemia (CLL) is reportedly most common in the western world, particularly among the elderly, and is characterized by increased lymphocytes in the bone marrow and blood.[18] It is diagnosed based on a blood smear and immunophenotyping by flow cytometry, although advanced studies have found that single-cell profiling of CLL at diagnosis can give the best treatment.[18] Among all cases, CLL was found to rank third, with a total of 25 cases, accounting for 11.9% of the total. This subtype was ranked the fifth in a study conducted between 1999-2013,where it constituted 8.6% of patients.[5] Among all age categories, the subtypes that appeared most frequently in our findings were B-ALL, ALL of undetermined type, and ALL-L2, accounting for 20 (9.5%), 19 (9%), and 13 (6.2%) cases. Generally, ALL is considered the most common diagnosis in Saudi Arabia, based on the study conducted between 1999-2013.[5] Meanwhile, B-ALL is the hematological malignancy most commonly diagnosed during early childhood in Al-Madinah Al-Munawwarah of Saudi Arabia, with 121 (70.3%) cases.[12]

Ultimately, the subsequent subtypes of acute myeloid and lymphoid leukemia were shown to have rare occurrence and the most minimal occurrence rates across all age groups: The prevalence rates of different types of leukemia are as follows: AML-M3 (2.9%), ALL-L3 (1.9%), T-ALL (1.4%), AML-M4 (1.4%), ALL-L1 (1%), AML-M2 (1%), AML-M7 (1%), AML-M1 (0.5%), and AML-M5 (0.5%).Notably, AML-M4 was previously reported the second most common type in Al-Madinah Al-Munawwarah of Saudi Arabia.[12] In another study conducted in 2022 that found percentages of some other rare subtypes, T-ALL was reported to affect fewer cases (4.7%) than B-ALL, which agrees with our findings;meanwhile, AML-M3 was observed in 3.5% of patients with AML, AML-M5 in 2.3%, and AML-M2 in 1.2%.[12]

Complete blood count tests are considered primary tests in the laboratory and are used to detect indicative patterns in fundamental hematological parameters. These parameters include WBCs, RBCs, HB, platelet count, HCT, MCV, MCH, MCHC, RDW, and MPV. In leukemia, these parameters may have diagnostic significance depending on whether they are increased, decreased, or without significant change. Thus, it is critical to detect abnormalities in the CBC early in order to do further confirmatory tests such as bone marrow and flow cytometry. Early diagnosis leads to immediate treatment, which reduces morbidity and mortality.[19] In our results from the last 5 years (2018-2022), we noted WBC to be elevated (termed leukocytosis)in all primary subtypes of leukemia (CML, AML, CLL, ALL) on account of changes in the bone marrow and corresponding increase in leukocytes. The replacement of bone marrow by malignant cells also leads to low platelet count (thrombocytopenia) and low levels of hemoglobin and RBC count (anemia), except in the case of CML where platelet count is raised slightly (thrombocytosis). Similar findings were observed in a 2019 study by Munir, which reported elevated WBCs and decreased RBCs, HB, and platelet count except in the context of CML, where platelet count was increased because CML is a myeloproliferative illness.[19,20] Red blood cell distribution width is a measure of the variation in RBC size, and is expanded inpatients with leukemia on account of many factors as bone marrow dysfunction or anemia and common complications resulting from medications, impaired RBC production, or immune system disorders.[21] In our results, we found elevated RDW in leukemic patients, consistent with a prior report of elevated RDW for CML patients in the chronic phase.[22]

Abnormal liver function tests, specifically increased levels of ALP, AST, ALT, GGT, total bilirubin and direct bilirubin, can be seen in patients with leukemia

due to many factors including direct infiltration of leukemic cells into the liver, chemotherapy toxicity, or infections.[23] Raised total bilirubin and direct bilirubin may suggest liver failure, as bilirubin is a waste product that the liver typically processes and excretes; meanwhile, albumin and total protein levels may be low in leukemic patients due to liver impairment.[23] Leukemia can affect the kidneys and produce elevations in urea and creatinine, which are waste products created by the liver and removed by the kidneys; creatinine is also created by muscles.[23] In our study, we noticed some changes in the liver and renal function of leukemia patients, specifically elevated levels of total bilirubin and the liver enzymes AST, ALP, and GGT, alongside reduced albumin. A notable exception was in cases of T-ALL, which exhibited no significant changes in total bilirubin and liver enzymes, just increased creatinine level and decreased albumin. Alanine transaminase, AST, and total bilirubin have been reported elevated in patients with acute leukemia before treatment and denote impacts on liver enzymes.[24] In this study, patients with AML, CLL, or B-ALL additionally exhibited increased levels of direct bilirubin, ALT, and urea; those with AML or CLL also had low levels of total protein, while patients with CLL or B-ALL showed increased levels of creatinine. Elevated creatinine and urea were previously reported in another study of patients with ALL; that study also observed increased liver enzymes (ALT, AST) due to renal and liver damage in leukemia patients.[23] In 2018, a study carried out by Singh et al[25] evaluated liver function in leukemia patients and concluded that both ALP and ALT increased in AML patients, whereas only ALP increased in ALL patients and slightly increased in CML patients; no significant changes in ALT and ALP were seen in CML patients. Meanwhile, AML patients in our study exhibited no significant change in creatinine levels, but Jumaah et al[26] reported in a 2021 study in Iraq that creatinine levels were increased in AML patients compared with controls.[26]

Regarding coagulation profiles, leukemic patients are predisposed to various coagulation abnormalities, including alterations in PT, APTT, and INR that result from abnormalities in clotting factors.[27] The specific effects can vary depending on the type and stage of leukemia, as well as other individual factors.[28] In patients with CML and with AML, we found significant increases in PT and INR. Those with CML also exhibited increased APTT. A prior study of patients with AML showed significant increase of PT and APTT, similar to our results, as did another in CML patients.[29,30] Another study that agrees with our results reported that patients with CML had a higher prevalence of abnormal PT and abnormal APTT compared to healthy controls, which the authors suggested may be due to the effects of CML on the production and function of clotting factors. The prolongation of PT in CML patients is attributable to reduced levels of Factor VII; meanwhile, prolonged APTT may be due to deficiency of Factor VIII.[30]

Finally, we observed no significant changes of coagulation profile in patients with CLL, B-ALL, or T-ALL. This contrasts with a prior study that reported increased PT and APTT in ALL patients compared with a control group; such increase might be related to chemotherapy-associated decreases in coagulation factors.[31]

Study limitations. This study investigated the prevalence and hematological characteristics of hematological malignancies in the southern region of Saudi Arabia. A potential limitation of the study is its sole reliance on data acquired from a single hospital for the patients being investigated. It is conceivable that more cases originating from the local region may be transferred to larger medical facilities, hence potentially resulting in an underestimating of the actual prevalence.

In conclusion, we assessed the hematological, biochemical, and coagulation profiles of these patients to identify significant changes. We found the incidence of leukemia to be higher in males than females, and chronic myeloid leukemia to be the subtype with the highest incidence in this region, out of a total 15 subtypes diagnosed. In addition, we found most types of leukemia that occur in southern Saudi Arabia to be associated with significant changes in patient hematological, biochemical, and coagulation profiles.

Additional research utilizing routine tests alongside the new technology and gene expression data could boost the accuracy of identifying and diagnosing leukemia. This could lead to improved disease detection, more precise diagnoses, timely intervention, and ultimately, increased patient survival rates and less comorbidities.

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