Research Article

World Journal of Hematology and Oncology

Prevalence And Associated Factors Of Adverse Blood Transfusion Reaction Among Transfused Patients At Bishoftu General Hospital, Oromia, Ethiopia: A Cross Sectional Study.

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Received Date: 02 July 2024
Accepted Date: 16 July 2024
Published Date: 22 July 2024

Citation:
Dereje Abebe Regassa. Prevalence And Associated Factors Of Adverse Blood Transfusion Reaction Among Transfused Patients At Bishoftu General Hospital, Oromia, Ethiopia: A Cross Sectional Study. World Journal of Hematology and Oncology 2024.

1. Abstract

1.1. Background: The magnitude variation of TRs, and inadequate implementation of hemovigilance systems is common in Ethiopia.This study aimed to determine the prevalence and associated factors of adverse blood transfusion reactions at Bishoftu General Hopsital, Ethiopia.

1.2. Methods: A cross-sectional study was conducted from July to December, 2023. Collected data were checked for completeness and consistency, then entered into Epi-Data version 3.1, then exported to (SPSS) software version 25 for analysis purpose. The socio-demographic and clinical characteristics were summarized by descriptive statistics, presented in tables,figures and texts. Bivariate and multivariate binary logistic regression analyses were conducted.AP-value <0.05 was considered statistically significant.

1.3. Results: Adverse blood transfusion reactions were seen in 5.6% of patients of the total,most of them developed Febrile nonhemolytic transfusion reaction (FNHTR), accounting for 48% of the cases and allergic reactions accounted for 36%. It was associated with a history of abortion (AOR=4.3;95%CI:1.3 13.8), unstable pretransfusion clinical status (AOR=3.1;95%CI:1.1 8.6), Transfusion history (AOR=5.42;95%CI:1.29 22.7), longer storage time AOR=4.6 (1.24 17.3), and receiving four or more units of blood (AOR=5.1; 95%CI:2.5-9.6).

1.4. Conclusion: Adverse blood transfusion reactions (ATRs) were seen in 5.6% of patients. of the total, 48% were Febrile nonhemolytic transfusion reaction (FNHTR), cases and allergic reactions accounted for 36%. Patients with history of abortion transfusion history, patients whose pretransfusion clinical status unstable, transfused with blood stored >20 days, and multi transfused patients should closely monitered.

2. Keywords:
Adverse Blood Transfusion Reaction, Transfusion, Transfusion Outcome, Ethiopia

3. Introduction

3.1. Background Information

Blood is the essence of life, a complex fluid medium of plasma containing a suspension of living cells [1]. The process of transferring homogenous blood from one member of the same species to another is known as blood transfusion. In human medicine, preserving severely ill patients with low blood parameters is a regular procedure that has been utilized for many years as an emergency and life-saving measure [2]. Red blood cell transfusions are employed for the treatment of bleeding and enhancement of oxygen delivery to tissues. The decision to administer red blood cell transfusions should be made based on the patient's clinical status. Reasons for red blood cell transfusion include symptomatic anemia (which may lead to shortness of breath, dizziness, congestive heart failure, and reduced exercise capacity), acute sickle cell crisis, and acute blood loss exceeding 30 percent of blood volume [3]. Fresh frozen plasma infusion can be utilized to counteract anticoagulant effects. Platelet transfusion is advised to prevent bleeding in patients with thrombocytopenia or platelet function abnormalities. Cryoprecipitate is used in instances of hypofibrinogenemia, which commonly occurs in cases of extensive bleeding or consumptive coagulopathy [3].

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BTR can be broadly divided into infectious or noninfectious, immunological or nonimmunological, immediate or delayed, and mild or severe. The classic symptoms of all types of BTR include fever, chills, and urticaria [4]. Although the implementation of good manufacturing practices (GMP) and suitable the rapeutic protocols has led to advancements in transfusion safety, it is important to acknowledge that blood and blood component transfusion can still result in adverse effects. These effects can be categorized as either acute, occurring within 24 hours, or delayed, manifesting after 24 hours [4]. A cute or delayed adverse reactions are categorized as either immunological or non-immunological. Acute adverse immunological transfusion reactions encompass Immediate (acute) hemolytic transfusion reaction (AHTR), Febrile nonhemolytic transfusion reaction (FNHTR), anaphylactic reactions, and Transfusion-related acute lung injury (TRALI). On the other hand, acute nonimmunological transfusion reactions consist of infection or sepsis, and circulatory overload. Delayed adverse transfusion reactions that fall under the immunological category include delayed hemolytic transfusion reaction, other delayed reactions, minor/major allergic reactions, anaphylaxis, erythrocyte and platelet alloimmunization, hemolytic reactions, post-transfusion purpura, immunomodulation, and graft versus host disease. Nonimmunological delayed transfusion reactions involve Transfusion transmissible infections (TTIs) such as HIV/HBV/HCV, and Transfusion-associated circulatory overload (TACO) [5].

The assessment of an ATR involves clinical findings such as physical examinations and vital signs, as well as laboratory investigations which encompass ABO and RhD grouping, re-cross matching, complete blood count (CBC), direct anti-globulin testing (DAT),evaluation for hemoglobinuria, elevated indirect and direct bilirubin test, as well as red blood cell (RBC) irregularities, such as schistocytes in cases of intravascular hemolysis or spherocytes in instances of extravascular hemolysis[6]. Blood is obtained only from low-risk voluntary donors who are not remunerated, and strict adherence to good laboratory practices helps in reducing the risk of transfusion reactions [7]. Nevertheless, every blood product is associated with the potential for transfusion reactions [8].These reactions can occur either as an immune response to the antigens present on blood cells or as a non-immune response resulting from an overload in circulation, transfusion siderosis, or transmission of infections [9,10]. The reactions may manifest as either an immune response to the antigens found on blood cells or a non-immune response caused by issues such as excessive circulation, transfusion siderosis, or the spread of infections [11]. The type and severity of transfusion reactions vary depending on the transfused blood product, the clinical condition of the recipient, their past medical history, and their age [12].The likelihood of their occurrence is 1000 times greater than that of complications arising from blood transfusion infections [3].In 2009, a survey on blood collection and usage across the United States revealed that over 60,000 transfusion reactions occur each year, with 16,000 of these reactions classified as serious [13]. The negative consequences of transfusions may lead to death and illness, affecting the individual as well as society and the economy [9].

In developing nations, close to 400,000 individuals receive treatment with blood donations provided by volunteers [14]. Despite various research efforts, there remains a lack of adequate direction regarding blood transfusions in underdeveloped nations. An investigation into the execution of hemovigilance in Sub-Saharan Africa revealed a rise in the reporting rates of transfusion adverse events from 1.1 to 16.1% per 1000 units [15]. In 2014, the incidence of transfusion-related mortality was 5.6 per million blood products, while there was a notable morbidity rate of 63.5 per million units of transfused blood [16]. One-third of blood donors experience adverse transfusion reactions (ATRs), which can occur unexpectedly. While most ATRs are minor, they have the potential to be severe. The most frequently reported unwanted reactions following blood donation are bruising (23%), a sore arm (10%), fatigue (8%), and vasovagal reactions (7%). Rare reactions include nerve irritation (0.9%), syncope (0.1-0.3%), and arterial puncture (0.01%) [16]. Based on a study regarding blood safety and supply in Africa, it was found that among the 46 countries involved, 82.6% had established and implemented a national blood safety policy, 71.7% had a plan for executing their national blood transfusion policy, 41.3% had legislation concerning blood safety, 73.9% had national protocols for the medical utilization of blood products, and merely 28.3% had tangible blood and blood product reserves [17].

Diverse strategies exist to mitigate the risks associated with blood transfusions. An important approach involves the utilization of autologous blood components, a method that has seen a rise in adoption over the past ten years [18]. An alternative approach to mitigating the hazards associated with blood transfusions is by implementing the hemovigilance program. Hemovigilance encompasses the provision of comprehensive care to individuals receiving blood or blood products, intending to prevent complications arising from transfusions, including sepsis, hemolytic reactions, acute pulmonary damage, bacterial infection, allergic reactions, and more. This program has proven to be highly effective in minimizing the occurrence of complications related to blood transfusions [19]. Many developed nations have implemented surveillance systems to oversee and identify severe adverse events or reactions linked to blood transfusion, as an integral component of their national hemovigilance systems [20]. Nevertheless, the implementation of hemovigilance systems in sub-Saharan Africa (SSA), including Ethiopia, is still lacking or inadequately established, except for a few nations like South Africa. In the majority of SSA countries, hemovigilance practices are limited to individual hospitals or clinical settings [20]. Patients who have received multiple blood transfusions and women who have given birth multiple times are susceptible to adverse transfusion reactions (ATRs). Individuals who have undergone numerous transfusions are particularly prone to experiencing febrile reactions, whereas older patients and those with cardiovascular conditions are at an increased risk of developing volume overload. Within low- and middle-income nations, one of the most commonly transfused demographics consists of women between the ages of 15 and 45 years [17]. ATRs tend to be more prevalent in female individuals and in patients who have undergone whole blood transfusions. The frequency of transfusions is affected by a range of factors such as gender, age, pre-

existing hematological abnormalities in complete blood count (CBC) findings, the clinical severity of the underlying disease, the duration for which the transfused blood has been stored, and the patient's history of prior transfusions. Furthermore, variables that may influence the outcomes or potential complications of blood transfusions encompass factors like a history of abortion, vital signs, the specific type of blood component being transfused, and the number of units being transfused [21]. There is a suggestion that the repetitive administration of blood transfusions may lead to an increased incidence of morbidity associated with transfusions [22].

Out of the adverse reactions that were reported, 25% were classified as serious, leading to a total of 368 deaths. Among the 284 infections transmitted through transfusion, 187 were caused by bacteria, 84 were viral infections, and 13 were either parasitic or fungal infections, resulting in nine deaths. Adverse reactions associated with the respiratory system, such as transfusion-associated circulatory overload, transfusion-related acute lung injury, and transfusion-associated dyspnoea, accounted for 8.3% of all reported adverse reactions, 20.1% of the serious cases, and 52.2% of the deaths [23]. The frequency of adverse transfusion reactions differs across various nations. For instance, the reported rate in the United States of America (USA) is 0.23% [24], in Bangladesh, it is 3.6% [25], and in Israel, it is 11% [26]. However, the rate ranges from 2.6% [20] in Congo,5.2% [21] to 6.6% [27] in Ethiopia, and 26.2% in Nigeria [28] among African nations. Though, blood transfusion is utilized in preserving severely ill patients for many years as an emergency and life-saving measure; it is associated with the potential for transfusion reactions. The reports of previous studies on the magnitude of this reaction are also different from the worldwide, and the implementation of hemovigilance systems in sub-Saharan Africa (SSA), including Ethiopia, is still inadequately established. Therefore, this study aimed to determine the prevalence and associated factors of adverse blood transfusion reactions among transfused patients at Bishoftu General Hopsital, Oromia, Ethiopia.

4. Methods And Materials

4.1. Study Design,Period and Area

A hospital-based prospective cross-sectional study was conducted at Bishoftu General Hospital from July 1st to December 30th, 2023.Bishoftu General Hospital is one of the best hospitals in the Oromia Regional State (ORS) and is located in Bishoftu town 47 kilometers southeast of Addis Ababa. The town is situated at an altitude of 1950 meters above sea level, at 90N latitude and 400E longitude [29]. There are two public hospitals, five health centers, two private hospitals, and ten private clinics; in the area, providing a range of medical services from preventive to advanced care. Established in 1948, Bishoftu General Hospital currently serves approximately 1.2 million people with services including [30] chronic care, emergency care, ART services, surgical procedures, dental care, medical services, ophthalmology, pediatrics, gynecology & obstetric, radiology, physiotherapy, pathology services, orthopedics, hematology oncology, pharmacy, laboratory, and others. This study was conducted in the central laboratory of Bishoftu General Hospital.

4.2. Study Population, Inclusion and Exclusion Criteria

The study population consisted of patients at Bishoftu General Hospitals who met the eligibility criteria and received a blood transfusion during the study period. To minimize the impact of confounding variables, certain patients were excluded from the study. These included patients who were under the influence of anesthetic drugs, unconscious during data collection, critically ill transfused patients, those who required blood transfusion during surgery, patients who received a blood transfusion within 24 hours after surgery, and patients undergoing hemodialysis. Additionally, only patients who provided consent at our facility were included in the study.

4.3. Sample Size Determination and Sampling Technique

During the study period, our research included a cohort of 450 patients who met the eligibility criteria and received blood and blood components. The data collection process employed a consecutive sampling technique to ensure a representative sample.

4.4. Data collection Material and procedure

4.4.1. Socio-Demographic and Clinical Data Collection Procedures

Appropriate socio-demographic information (such as age, gender, place of residence, and marital status background) along with detailed medical history encompassing transfusion records, instances of transfusion, abortion history, frequency of abortions, pregnancy background, and gravidae were obtained via structured questionnaires. Data regarding the transfusion department, transfusion occurrences, primary diagnosis, average duration of blood transfusion, blood components, duration of blood and its components storage, quantity of units transfused, presence or absence of transfusion adverse reactions, types of transfusion reactions, and the nature of these reactions were gathered using checklist sheets. A comprehensive physical and clinical assessment was carried out on all participants before the commencement of the transfusion. Baseline data, including vital signs such as body temperature, blood pressure, pulse rate, respiratory rate, and oxygen saturation percentage, were measured and documented on the data collection checklist. Throughout the transfusion process, vital signs were closely monitored within 15 minutes post-initiation, followed by regular checks every half an hour until the completion of the transfusion, and subsequently at 4-hour intervals for the next 24 hours. Additionally, patients were carefully examined and their signs and symptoms of adverse transfusion reactions (ATRs) were documented.

4.5. Laboratory Examinations

Data regarding the date of blood donation, blood group of both the donor and recipient, number of units transfused, and type of blood component were meticulously documented using a data collection checklist sourced from the transfusion service center logbook and patient chart. Blood and urine samples were procured from each patient both before and after the transfusion to investigate Adverse Transfusion Reactions (ATRs)

in suspected cases. Pre-transfusion Complete Blood Count (CBC) and Direct Antiglobulin Test (DAT) outcomes were gathered either from the patient's medical record or requested for those lacking such information. The majority of the study participants had pre-transfusion CBC results available in their medical records, while for a small number of patients without CBC results, the investigator made specific requests. Notably, none of the patients had DAT results documented in their medical records. The initial complete blood count (CBC) and direct antiglobulin test (DAT) were carried out using a sample obtained for cross-matching purposes for individuals lacking this information in their medical records. Before the cross-matching procedure, the CBC was assessed using five differential Hematological analyzers, specifically the Sysmex-500i and Sysmex XN550 machines from Sysmex in Germany, at the Bishoftu Central Hematology Laboratory.

All pre-transfusion cross-matches were carried out utilizing immediate-spin methods. Nevertheless, in cases where patients were suspected of experiencing a transfusion reaction, pretransfusion samples underwent re-cross-matching employing the polyclonal antihuman-globulin (AGH) technique in conjunction with post-transfusion samples. The direct antiglobulin test (DAT) was executed by combining the washed RBCs of the patient post-transfusion with polyclonal AGH sera to identify any in vivo sensitization of the patient's RBCs. Furthermore, a 5ml urine specimen was obtained in a sterile urine cup to determine pre-transfusion urine hemoglobin (Hb) levels using a urine strip test. Patients suspected of acute transfusion reactions (ATRs), either clinically or through urine Hb screening, underwent verification of their blood pack labels or patient identity. The pre-transfusion sample of these patients was subsequently retested for their ABO and Rh blood type. Following this, three mL of post-transfusion blood specimen was obtained from the suspected patients and placed in a tri-potassium ethylenediaminetetraacetic acid (K2-EDTA) test tube. This sample was utilized for CBC, malaria parasite screening, regrouping, re-cross match, and screening for in vivo sensitization of RBCs (DAT). Before analysis, the collected blood sample was assessed for proper labeling, hemolysis, and clotting. Furthermore, a five mL urine specimen was gathered in a clean urine cup container to determine post-transfusion urine Hb levels. The donor blood sample was also subjected to blood culture, regrouping, and cross-match. In cases where hemolysis was suspected, a blood smear examination was conducted to identify the type of hemolysis.

4.6.Data Quality Management

To guarantee the accuracy and reliability of the data, the questionnaires and checklists in English were translated into the local language and subsequently retranslated back into English. This meticulous process aimed to ensure both the precision and consistency of the information gathered. Additionally, a comprehensive half-day training session was conducted for the four data collectors, consisting of two laboratory technologists and two clinical nurses. The training covered essential aspects such as the study objectives, data collection procedures, and the importance of maintaining confidentiality. The purpose of this training was to minimize any potential technical or observation bias that could affect the data collection process. During the study period, the quality of socio-demographic and clinical data was upheld by conducting daily checks for completeness and consistency through on-site supervision of data collectors. Confidentiality of study participants' test results was ensured through the use of codes, and records were securely stored in a secluded location. Feedback and necessary corrections were given following the daily data collection process. The laboratory test results were upheld to a high standard by adhering to the manufacturer's instructions and standard operating procedures throughout the process of specimen collection, CBC analysis, Direct immunoglobin test (DAT), and blood film preparation and examination. To prevent hemolysis after collection, the blood sample was carefully dispensed onto the walls of a K3-EDTA test tube, gently mixed by inverting it 8-10 times, and subsequently analyzed for CBC. A thin blood film was meticulously prepared, appropriately labeled, air-dried, and then stained with Wright stain to assess the type of hemolysis. Acceptance criteria for collected samples such as non-hemolysis, non-clotting, and adequate sample volume were checked. To avoid mix ups after collection, labeling was done on both the sample holder and the request paper with the same identification code. According to the hospital laboratory protocol, low, normal, and high control materials were used for the hematology analyzer. Background readings were obtained daily to reduce background carryover effects. Reagent expiration dates were checked before analyzing patient samples. All laboratory assays were analyzed within 2 hours of sample collection, and all test results were recorded and reported and samples were properly managed.

4.7. Statistical Data Analysis and Interpretations

Collected data were checked for completeness and consistency, then entered into Epi-Data version 3.1 (Epi-Data Association, Denmark), and exported to Statistical Package for Social Sciences (SPSS) software version 25 (IBM SPSS Statistics, USA) for analysis purposes. The normality of continuous data distribution was assessed using Histograms, Kolmogorov-Smirnov and Shapiro tests. Descriptive statistics were utilized to summarize the socio-demographic and clinical characteristics of the study participants, presented in tables, figures, and texts. Bivariate and multivariate binary logistic regression analyses were conducted to determine the association between dependent and independent variables. The multivariate binary logistic regression model was analyzed using backward likelihood and stepwise methods for variables with a P-value of < 0.25 in the bivariable binary logistic regression. The model fitness of the final multivariate logistic regression was assessed using the Hosmer and Lemeshow test. A P-value <0.05 was considered statistically significant.

4.8. Ethical Consideration

Before commencing the study, the researchers obtained official ethical clearance from the local Institutional Review Board, with reference number BEFO176992/2023GC. This ethical clearance was then submitted to the administration office of Bishoftu General Hospital, as well as to the respective department head offices. Once permission was granted by the Hospital Administrator and the heads of various

departments, a comprehensive explanation of the study's objectives, procedures, potential benefits, possible risks, and the voluntary nature of participation was provided to all participants. Subsequently, written informed consent was obtained from each individual involved in the study. To ensure the confidentiality of the collected data, codes were used instead of participants' names, and strict measures were implemented to prevent unauthorized access to the data. It is important to note that our study adhered to the principles outlined in the Helsinki Declaration (64th WMA General Assembly).

5. Result

5.1. Socio-Demographic and Clinical Characteristics Of The Study Participants

In this study, a total of 450 individuals were recruited. Among them, one-hundred fifty-seven (34.9%) participants were in the age range of 26-45 years. The majority proportion of the study sample, comprising 274 individuals (60.9%) were female. Furthermore,283 participants (62.9%) resided in rural areas.Regarding marital status, the majority of the participants,198 individuals (44%), were single, while 195 individuals (43.3%) were married (Table 1).

Table 1: Socio-demographic characteristics of the study participants at Bishoftu General Hospital, Oromia, Ethiopia(n=450).

Variables	Categories	n(%)
Age	<18 yrs	39(8.7%)
	19-25 yrs	115(25.6%)
	26-45 yrs	157(34.9%)
	46-65 yrs	107(23.8%)
	>65 yrs	32(7.1%)
	Age mean: 37.42+16.1	
Sex	Male	176(39.1%)
	Female	274(60.9%)
Residence	Urban	167(37.1%)
	Rural	283(62.9%)
Marital status	Single	198(44%)
	Married	195(43.3%)
	Divorced	9(2%)
	Widowed	48(10.7%)

Key Note: Data are expressed in frequency(percent).

5.2. Clinical Characteristics of Our Study Participants

Among the participants in the study, a total of 199 individuals (72.6%) had a history of pregnancy. Out of these,71 individuals (35.7%) had a previously undergone an abortion. Among those who had history of abortion,the majority (77.5%) had undergone the procedure once, while a smaller percentage had undergone it two or more times. In terms of transfusion indicators, our study, maternal complications 30.4% were the most common, followed by cases related trauma, orthopedic, and surgery (22.4%). Hematological disorders accounted 18.4% of cases, while chronic diseases accounted for 17.1%. The least common transfusion indicator was gastrointestinal bleeding,accounting for 11.6% of cases. The majority of transfusion procdures were performed in emergency ward with 192 cases (42.7%). The surgical ward accounting for 137(30.4%),while Gynecology/Obstetrics ward had 54 cases (12.0%). Among the transfused patients,a total of 252 individuals (56%) were deemed stable according to the clinical assessment conducted prior to the transfusion.Within the study participants, 183 individuals (40.7%) had a history of previous transfusions.Among these individuals ,105(57.4%) had undergone two transfusions, 46(25.1%) had undergone one transfusionand the remaining 32(17.5%) had received three or more transfusions (Table 2).

Table 2: Clinical characteristic of study participants at Bishfotu General Hospital, Oromia, Ethiopia (n=450).

Variables	Categories	n(%)
History of Pregnancy	No	75(27.4%)
	Yes	199(72.6%)
Gravidea	One	104(52.3%)
	two	79(39.7%)
	Three and more	16(8.0%)
History of abortion	No	128(64.3%)
	Yes	71(35.7%)
Frequency of abortion	One times	55(77.5%)
	Two times	14(19.7%)
	Three and more	2(2.8%
Primary diagnosis	Maternal complication	137(30.4%)
	Trauma,Orthopedic,and surgical case	101(22.4%)
	Chronic disease cases	77(17.1%)
	Hematological cases	83(18.4%)
	Gastrointestinal bleeding	52(11.6%)
Ward at which transfusion done	Emergency	192(42.7%)
	Gyn/Obs	54(12.0%)
	Medical ward	28(6.2%)
	Pediatric	39(8.7%)
	Surgical	137(30.4%)
Pretransfusion clinical status	Not-stable	198(44%)
	Stable	252(56%)
Transfusion history	No	267(59.3%)
	Yes	183(40.7%)
Transfusion history frequency	One times	46(25.1%)
	Two times	105(57.4%)
	Three and more times	32(17.5%)

5.3. Characteristics and Type of Transfused Blood Component with Proportion of Transfused Patients

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A total of 769 blood components were administered to 450 patients, resulting in an average of 1.71 units per patient. The average number of units transfused was higher for males at 4.37 compared to females at 2.81. The majority of patients received whole blood transfusions, accounting for 337(74.9%), followed by packed red blood cells (PRBC) at 66 (14.7%), and concentrated platelets at 47(10.4%). Among the transfused patients, 220(48.9%) had transfusion procedures lasting an hour,while 187(41.5%) lasted less than thirty minutesand 43(9.6%) lasted more than an hour.Most participants, 324(72%), received one unit of blood, while 92(20.4%) received two to three units, and 34(7.6%) received more than four units (Table 3).

Table 3: Characteristics and type of transfused blood component with proportion of transfused patients at Bishoftu General Hospital, Oromia, Ethiopia (n=450).

Variables	Categories	n(%)
Blood component transfused	Whole blood	337(74.9%)
	Concentrated Platelet	47(10.4%)
	Packed RBC	66(14.7%)
Age of transfused blood in days	<20days	288(64%)
	>20days	162(36%)
Average of time taken for transfusion(min)	30 to 60 minutes	234(52.0%)
	Less than 30 minutes	170(37.8%)
	More than 60 minutes	46(10.2%)
Number of blood unit transfused	One bag	325(72%)
	Two to three bags	88(19.6%)
	Four and more bags	37(8.2%)
Mangitude of transfusion reaction	No	425(94.4%)
	Yes	25(5.6%)

5.4. Types, Sign And Symptoms Of Transfusion Reaction Among Transfused Patients

Figureillustrates the distribution of transfusion reaction based on their respective types among individuals who experienced TRs. The most prevalent type of transfusion reaction observed was febril non-hemolytic transfusion reaction (FNHTR), which occurred in 12 patients, accounting for 48% of the total.This was followed by allergic reactions in 9 patients (36%), Transfusion related acute lung injury (TRALI) in 2patienst (8%), anaphylactic reaction and transfusion as associate dyspnea (TAD) in 1 patient each (4%), respectively. Fever was the predominant clinical sign among acute transfusion reaction (ATRs), with 32% cases,followed by urticaria in 4(16%), Skin rash and pruritis in 3(12%), nausea/vomiting and tachycardia accounting 2(8%), and chills/rigor, hypotension anad hypertension accountign for each accounting for 1(4%) cases (see Figure 2).

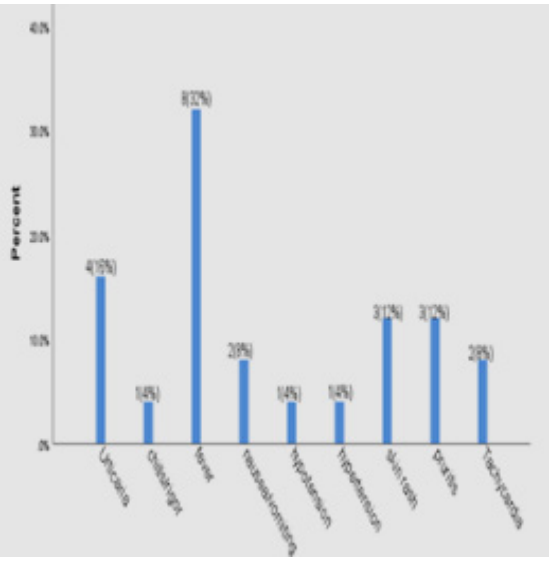

Figure 2: Sign and symptoms of adverse transfusion reaction

5.5. Transfusion Reaction and Associated factors

A total of 25 cases of acute transfusion reactions (ATRs) were reported,represented a prevalence rate of 5.6% among ATRs. The majority of these reactions were classified as febrile non-hemolytic transfusions reactions (FNHTR), accounting for 48% of the cases. Allergic reactions accounted for 36% of the cases(refer to figure 1). Notable, the prevalence of ATRs was higher in females compared to males, with rates of 7.3% and 2.9% respectively.

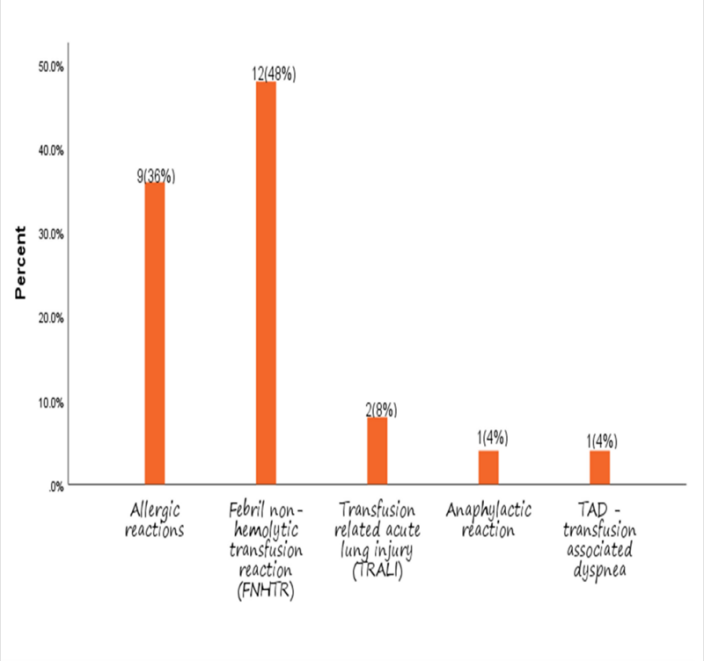

Figure 1: Types of adverse transfusion reaction

Furthermore, ATRs were more commonly observed in patients with a history of transfusion (9.3% vs 3%),patients who had experienced pregnancy (8.7% vs 2.7%), patients with a history of abortion (15.5%

vs 5.5%), and patients with an unstable pretransfusion clinical status (8.6% vs 3.2%). The prevalence of ATRs also varied based on the number of blood units transfused, with rates of 17.7% for patients receiving mor than 4 units, 8.7% for patients receiving two to three unitsand 3.4% for receiving one unit. Additionally, the duration of transfusion played a role, with rates of 17% for transfusions lasting more than one hor, 4.7% for those lasting less than thirty minutesand 3.8% fot those lasting one hour. Interestingly, approximately 9.3% of ATRs occurred in patients who received blood that had been stored for a long duration. In bivariate binary logistic regression analysis, ATRs showed association with a history of abortion (COR=3.2;95%CI:1.2 8.6), unstable pretransfusion clinical status (COR=2.9;95%CI:1.2 6.8), transfusion history (COR=3.32;95%CI:1.4-7.9), storage time greater than 20 days (COR=2.84(1.4-6.5) and transfusion of 4 or more units of blood or blood components (COR=8.4;95%CI:2.25-21.6). Upon adjusting for the effects of confounding factors in the multivariate model, a history of abortion (AOR=4.3;95%CI:1.313.8) unstable pretransfusion clinical status (AOR=3.1;95%CI:1.1 8.6), Transfusion history (AOR=5.42;95%CI:1.29 22.7), storage time greater than 20 days (AOR=4.6(1.24 17.3), and transfusion of 4 or more units of blood or blood components (AOR=5.1;95%CI:2.5-9.6) were found to be significantly associated with ATRs.

6. Discussion

The process of transferring homogenous blood from one member of the same species to another is known as blood transfusion. In human medicine, preserving severely ill patients with low blood parameters is a regular procedure that has been utilized for many years as an emergency and life-saving measure [2]. Blood is obtained only from low-risk voluntary donors who are not remunerated, and strict adherence to good laboratory practices helps in reducing the risk of transfusion reactions [7]. Nevertheless, every blood product is associated with the potential for transfusion reactions [8]. In 2014, the incidence of transfusion-related mortality was 5.6 per million blood products, while there was a notable morbidity rate of 63.5 per million units of transfused blood [16]. Many developed nations have implemented surveillance systems to oversee and identify severe adverse events or reactions linked to blood transfusion, as an integral component of their national hemovigilance systems [20]. Nevertheless, the implementation of hemovigilance systems in sub-Saharan Africa (SSA), including Ethiopia, is still lacking or inadequately established, except for a few nations like South Africa. In the majority of SSA countries, hemovigilance practices are limited to individual hospitals or clinical settings [20]. The present investigation revealed that the overall prevalence of adverse blood transfusion was 5.6% in the population of patients who received blood transfusion. This estimate was accompanied by a 95% confidence interval ranging from 3.6% to 8.1%. The results of this study align with previous research conducted in Belgau (4.41%) [31],Japan (5.05%) [12], Iran (4%) [16], Ethiopia (5.2%) [21]. While, the current study results was higher than studies done in Taiwan (3.5%) [32], India (3.4%) [33], Nigeria (3.6%) [34], Democratic Republic of Congo (3.4%) [22], Japan (2.6%) [35], Democratic Republic of Congo (2.6%) [20], Iran (0.95%)[36], (0.4%) [16], India (0.3%) [37], (0.4%) [38], (0.96) [39], (0.27%) [40], (1.17%) [41], (0.92%) [42], Pakistan (0.38%) [43], (0.17%)[44], (0.75%)[45], Australia (0.24%) [46], China (1.35%)[47] and Eriteria (0.42%) [48]. The disparities noted in our investigation in comparison to prior research could be ascribed to variations in the types of blood components used for transfusion. For example, in Iran, leukocyte filtration was employed, while our study utilized only whole blood, which contains elements that have the potential to incite transfusion reactions [49]. In Japan, leukocyte-reduced blood components were utilized, whereas in our current study, non-leukocyte reduced blood components were used. Febrile transfusion reactions that are non-hemolytic typically arise from the discharge of cytokines from leukocytes found in transfused red blood cells or platelet components, leading to symptoms like fever, chills, or rigors [50]. These cytokines, including interleukin-8, which acts as a chemotactic cytokine for neutrophils and eosinophils [51]. In non-leukocyte-reduced blood, cytokines are significantly elevated in stored blood component,they prompting leucocyte recruitment and provoking an allergic reaction, when such a blood component is transfused [52]. Another possible explanation could be that the majority of research studies relied on data from national hemovigilance reports, potentially leading to a reduction in the reported incidence rate. In India, the incidence rate is documented as 1 in 1412 when considering the uploaded data, and 1 in 743 when not taking the uploaded data into account [53].

The result of our study was found to be lower compared to similar studies conducted in Nigeria (26.3%) [28], Israel (11%) [26], Burkina Faso (8.4%) [54], Sweden (7.9%) [55] and Ethiopia (6.6%) [27]. This observed difference in findings could potentially be attributed to variations in the demographics of the study participants. For example, the study in Israel focused on elderly patients with a mean age of (82 ± 9), which could explain the higher incidence rate. In contrast, our study included participants with a mean age of (37.42 +16.1) years old. In Nigeria, all participants were pregnant women, with 86% being multigravid. Additionally, the transfusions administered mainly involved women who experienced incomplete abortion and placenta previa with fetal-maternal hemorrhage, which could be linked to ATR [28]. Multigravid women may develop alloantibodies to leukocyte or platelet antigens due to fetal-maternal hemorrhage. Consequently, women who develop leukocyte antibodies following pregnancy or abortion are at a higher risk of experiencing allergic reactions and FNHTR if they are subsequently transfused with leukocyte-containing blood components [56]. In the present investigation, the predominant form of acute transfusion reaction (ATR) observed was FNHTR, accounting for 48% of cases, while allergic reactions constituted 36%. These findings align with previous studies conducted in various countries, including Saudi Arabia [57], Nigeria [58], Zimbabwe [59], Eriteria [48], Democratic Republic of Congo [22], Australia [46], Pakistan [43], India [38,41,45,49], Bhutan [60] and France [61]. But,our research findings differed from those of studies conducted in various countries such as India (55.1% vs 35.7%) [62],(55.6%vs 33.3%) [37], Israel (45.5% vs 19.5%) [26], Japan (70% vs.13.1%) [35]

and Malaysia (50.2% vs 38%) [63], Bahir Dar, Ethiopia (65% and 30%) [64], Iran (44% vs 42%) [16],Iran(53.5% vs 24%) [65], Iran (42.51% vs 37.17%) [66], China (86.67% vs 4.24%) [47] and Bangladesh (40.5% vs 36.4%) [25]. In these studies, allergic reactions were less frequently observed compared to our study.

As a result of the introduction of antigens, such as WBC, into the recipient's body, there is an increase in the production of cytokines, leading to the development of a febrile non-hemolytic transfusion reaction. Additionally, the infusion of cytokines from the donor, which are generated during storage, can also contribute to the onset of allergic responses and FNHTR in transfusion recipients. The allergic reaction is triggered by the recipient's immunoglobulin E or non-IgE antibodies reacting to proteins or other allergenic soluble substances present in the donor plasma. Examples of potential biological response modifiers include histamine, lipids, complement fragments, and cytokines. These substances can either arise during the storage of RBC or PLT products or be associated with transfusion reactions. However, it is important to note that there is currently no clinical evidence to support the claim that cytokines cause ATR, as their levels are low in products derived from preserved erythrocytes [67]. In the present investigation, two cases of transfusion-related acute lung injury (TRALI), one case of Transfusion-associated dyspnea (TAD), and one case of Anaphylactic reaction were observed, accounting for 8%, 4%, and 4% of the total adverse transfusion reactions (ATRs), respectively. Similar findings have been documented in previous studies conducted in various regions including Chandigarh India [49], Sikkim India [42], West Bengal, India [40], Tehran Iran [66], Bhutan [60], New Delhi India [62], Lahore Pakistan [45], Australia[48] and Eriteria [48].

In TRALI, the formation of antibodies against leucocytes (specifically polymorphous neutrophils [PMN]) can occur as a result of exposure to foreign antigens through pregnancy, transfusion, or transplantation. This immune response targets both neutrophils and human leucocyte antigen. Two distinct causes have been suggested to explain the development of TRALI [68]. A potential occurrence involving the infusion of anti-human leukocyte antigen (HLA) or antigranulocyte antibodies into patients with matching antigens can manifest as a solitary event mediated by a single antibody. In most instances, the antibodies originate from the donor rather than the patient. Another model explaining the mechanism of transfusion-related acute lung injury (TRALI) suggests a two-step process, wherein neutrophil activation leads to damage in the pulmonary endothelium, capillary leakage, and pulmonary edema. Notably, significant clinical improvement can be observed within 48-96 hours with prompt respiratory support [68]. Anaphylactic reactions can occur as a result of antibodies targeting various donor plasma proteins, such as IgA, haptoglobin, complement, and ethylene oxide. In individuals with IgA deficiency, anaphylaxis is frequently observed due to the presence of antibodies against donor IgA. Transfusion-associated dyspnea, on the other hand, is characterized by respiratory distress occurring within 24 hours of transfusion, which does not meet the criteria for TRALI, TACO, allergic reactions, or other identifiable causes [68]. In the present study, individuals with a previous record of abortion exhibited a 4.3-fold increased likelihood of developing ATR compared to those without any history of abortion. The process of abortion may result in the introduction of fetal antigens into the maternal bloodstream, thereby triggering sensitization. Subsequently, when a transfusion occurs, the immune system generates antibodies that can give rise to AHTR or FNHTR [69]. It is possible that the reason for this occurrence is the presence of women who have undergone abortions and subsequently develop alloantibodies against leukocyte, red cell, or platelet antigens due to fetal-maternal hemorrhage, whether it is overt or not. These antibodies, which are produced after pregnancy or abortion, have a higher likelihood of causing adverse reactions during blood transfusions, such as allergic reactions and febrile non-hemolytic transfusion reactions (FNHTR), when the patients receive blood components containing leukocytes [70].

The analysis conducted in our study has identified several factors associated with the occurrence of transfusion reactions. Specifically, we found that patients with a history of unstable pretransfusion clinical status were 3.1 times more likely to experience transfusion adverse reactions compared to the stable group ($p < 0.029$). It is important to note that evidence of immunological or allergic reactions to blood transfusions was observed in patients with unstable pretransfusion clinical status. This highlights the potential risk of provoking immune system responses and jeopardizing the overall prognosis of transfused patients. Therefore, all blood transfusions must be carried out under appropriate conditions by qualified healthcare providers, who should also closely monitor the preclinical status of patients before conducting the transfusion procedure. The occurrence of adverse transfusion reactions (ATR) was found to be significantly associated with the number of units of blood transfused per patient, as indicated by studies conducted in both the United States [71] and Nigeria [58]. This finding aligns with the current research. Specifically, compared to the transfusion of a single blood bag, the transfusion of two to three blood bags did not significantly increase the risk of transfusion responses. However, when four or more blood bags were transfused, the risk of transfusion responses increased by 5.1 times ($p = 0.003$). Patients who develop allergic transfusion reactions have developed sensitivity to the antigens present in the donated blood. These antigens are soluble, and the resulting reaction is dependent on the dosage. The fever is triggered by leukocytes and cytokines found in the donor blood. Consequently, the more units of blood are transfused, the higher the levels of leukocytes and cytokines that are introduced to the recipient. Therefore, febrile non-hemolytic transfusion reactions are more common in individuals who have undergone multiple transfusions. Antibodies against ABO blood group antigens or alloantibodies against other red blood cell antigens are formed following sensitization from a previous transfusion or pregnancy. In patients who receive multiple transfusions, sensitization is heightened due to exposure to various antigens [3].

There was a correlation observed between the duration of blood component storage and the incidence of ATR. Patients who received

long-stored blood (stored for ≥20 days) were 4.6 times more likely to experience an acute transfusion reaction compared to those who received short-stored blood. Similar results were reported in two separate studies conducted in northeastern Nigeria [28] and north-west Nigeria [34]. The former study compared stored blood with fresh blood, while the latter study suggested that the increased presence of leukocyte bio-chemicals in long-stored blood could be a contributing factor, as indicated by a study conducted in Taiwan [52]. Based on the findings of this research, a notable difference in leukocyte biochemicals was observed between pre-storage leukocyte-reduced and post-storage leukocyte-reduced blood components. The levels of IL-1β and IL-8 were notably higher in the post-storage leukocyte-reduced blood component. These bio-activators were linked to adverse transfusion reactions, particularly in cases of febrile non-hemolytic transfusion reactions (FNHTR) and allergic reactions [52]. In our investigation, the transfused blood components did not undergo leukocyte reduction, and the most commonly observed adverse transfusion reactions were allergic reactions and FNHTR. Therefore, these biochemical changes may be more pronounced in long-stored blood components, leading to a higher incidence of adverse transfusion reactions in patients receiving such blood. However, a conflicting report by Heddle NM et al. suggested that there was no significant impact on patient outcomes between short-stored and long-stored blood components. It is important to note that the focus of this study was on patient mortality post-transfusion, rather than the occurrence of transfusion reactions [72].Consequently, while long-stored blood may not be directly linked to patient mortality, it could still be associated with adverse transfusion reactions. In the present investigation, it was observed that patients with a history of previous transfusions were 5.42 times more prone to developing ATR compared to their counterparts. This increased susceptibility could be attributed to the sensitization of the immune system and the subsequent production of antibodies against specific blood cell antigens (RBC, WBC, and PLT) following prior transfusions. The presence of this sensitized immune system may lead to the occurrence of HTR or FNHTR in subsequent blood transfusions [73]. The American Society of Hematology has reported that alloimmunization to sickle cell disease and thalassemia can result in hyper-hemolysis during subsequent transfusions [74].The association between previous transfusions and TR was found to be statistically significant, aligning with findings from studies conducted in Bahir Dar, Ethiopia [64] and northwest, Nigeria [34].

7. Limitations Of This Study

The relationship between the explanatory variables and types of ATR was not examined due to the limited number of participants (n=25) who experienced the outcome of interest, ATR, for certain variables. This research solely focused on whole blood and blood component transfusions, potentially leading to an overestimation of transfusion reaction rates. Furthermore, individuals who developed AHTR were not evaluated for antibody screening, identification, and organ function tests.

8. Conclusion and Recommendation

The prevalence of adverse transfusion reactions (ATRs) was recorded at 5.6% overall. Among these reactions, the most commonly observed was febrile non-hemolytic transfusion-related reaction (FNHTR), accounting for 48% of cases, followed by allergic reactions at 36%. The remaining 8% of cases were attributed to transfusion-related acute lung injury (TRALI), while anaphylactic reactions and transfusion-associated dyspnea (TAD) each accounted for 4%. Several factors were found to have a statistically significant association with ATRs. These factors include prior transfusion history, history of abortion, unstable pretransfusion clinical condition of patients, prolonged storage time, and the number of blood units transfused. Therefore, it is important to closely monitor patients with a history of transfusion or abortion, as well as those with unstable pretransfusion clinical conditions, due to their increased risk of experiencing ATRs. To reduce the risk of transfusion reactions and ensure the safety of patients, it is essential to implement various measures. These measures include closely monitoring blood transfusions, optimizing the use of blood products, conducting extended phenotyping, and implementing leukoreduction of blood bags. Therefore, we recommend that future researchers conduct additional studies with a larger sample size, involving multiple centers, and also consider investigating the types of delayed acute transfusion reactions.

9. Acknowledgments

Our appreciation is extended to the personnel at Bishoftu General Hospital, along with the data collectors, supervisors, study participants, and questionnaire interpreters, for their indispensable assistance during the implementation of this research.

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