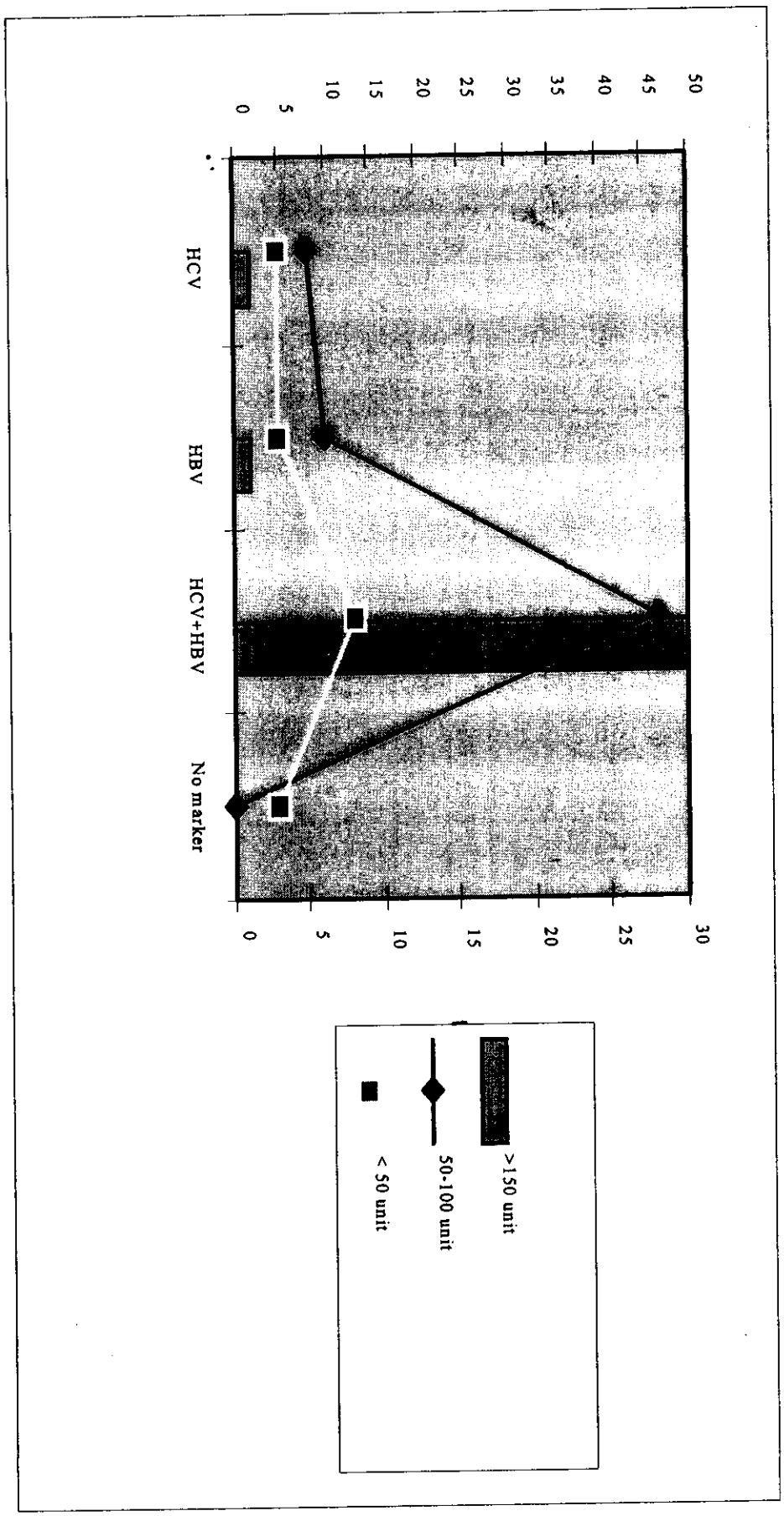
Table (18):Viral hepatitis serology in the multi-transfused groups according to No. of blood transfused units.

Hepatitis markers	*HCV*		*HBV*		*HCV+HBV*		*no marker*		*total*
No. Unit of blood	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	
>150 unit	*2*	*3.7*	*2*	*3.7*	*50*	*92.6*	*-*	*0*	*54*
50-100 unit	*5*	*12.8*	*6*	*15.4*	*28*	*71.8*	*-*	*0*	*39*
< 50 unit	*3*	*17.6*	*3*	*17.6*	*8*	*47.2*	*3*	*17.6*	*17*
Total	*10*		*11*		*86*		*3*		*110*

Table (18): Showed the more units of blood transfused to multi-transfused patients, the more prevalence of viral hepatitis infection. Where, combined HCV antibodies and HBV infection cases were more prevalent



Figure(18): Viral hepatitis serology in the multi-transfused groups according to No. of blood transfused units.

DISCUSSION

Multi-transfused infants and children are patients who had received two or more units of blood ***(Pineda et al., 1987).*** Blood transfusion is life long replacement in some hematological diseases such as thalassemia major, hemophilia, sickle cell anemia, aplastic anemia and others ***(Sher et al., 1993).*** A zero risk blood supply is not feasible, polytransfused subjects are at increased risk of contracting hepatitis ***(El Alfy, 1994).*** It is known that safest transfusion is no transfusion ***(Aoki et al., 1993).***

Thalassemia major is the commonest chronic hemolytic anemia in Egypt ***(Sabry, 1973).*** The primary management of thalassemic children depends on regular blood transfusion and iron chelating therapy ***(Weatherall, 1990).***

Chronic liver disease occurs frequently in polytransfused B. thalassemic children ***(Pastore et al., 1983)*** and are known to follow acute infection in the majority of cases ***(Coltorti et al., 1995 - Van Damme, 1995).***

A study population of 100 B. thalassemia major patients aged 3-15 years with a mean of 11.1± 3.3 was assembled to determine the prevalence of viral hepatitis markers B and C, and we select one
of the most sensitive liver function of surrogates to detect chronic liver disease which is ALT level. Abdomenal ultrasound was done for all the patients.

HCV is now a major public health concern ***(Gurakar et al.,1993)*** and is endemic world wide ***(Farci et al.,1995)*** and is a major health problem in Egypt ***(El Gohary, 1995).*** HCV is hyperendemic in Egypt ***(Darwish et al., 1996).***

There is relatively high prevalence of HCV antibody seropositivity in healthy Egyptian children compared to reports from other countries ***(el-Nanawy et al.,1995).***

HCV is blood-born virus and almost all post-transfusion hepatitis are caused by this virus ***(Komatsu et al., 1996).***

NANBH accounts for 90% of post-transfusion hepatitis before discovery of a test for antibodies to HCV ***(Iorio et al., 1993),*** and ten years ago, in Egypt, NANBH was determined to be 48% in polytransfused in a previous studies ***(Abdel Ghaffar 1983).***

Recent reports have indicated strikingly high rates of sero-positivity against HCV among Egyptian. Rates of HCV sero-positivity among blood donors (9.7% - 28%) ***(Darwish et al., 1993).*** Military recruits (22.1% - 33.4%) ***(Abdel Wahab et al., 1994),*** rural primary school children (12.1%) ***(Kamel et al., 1994).***

In our study, the prevalence of HCV antibodies was 88% (61% in males, 27% in females).

This is comparable to study was done by ***El Alfy et al.,(1997),*** who reported that 89% of their cases [135 multi-transfused thalassemic children] were contracting hepatitis C infection. Also ***Kamal et al., (1996),*** who reported that 87% of his cases (previously transfused females) acquired HCV antibodies and by ***El Alfy and Kamel in (1994),*** found that 80% of 120 B.thalassemic children had HCV infection. And by ***Saad (1992),*** found that HCV seropositivity in multi-transfused children was 82%. Also , in study was done by ***El Gohary et al;, (1995),*** found that the prevalence of HCV in thalassemic children was 75.6%, Western studies reported a prevalence of 76% HCV positive cases among polytransfused ***(Locasciulli et al.,1993).*** By study with ***Khalifa et al., (1993),***who denoted HCV seropositivity of 73% in multi-transfused thalassemic patients[RIBA confirmed].

In study with ***Congia et al., (1996),*** found that 74.7% of polytransfused thalassemic patients were infected with HCV after regular transfusion program. In Saudi Arabia, HCV infection was 70% ***(El Alfy and Gad Allah 1991 - Al Fawaz and Ramia 1993).***

Exposure to HCV was studied in 35 transfusion dependent cases of thalassemia major 60% of cases were anti-HCV positive***(Bhatti et al.,1995).***

Other studies were in contrast with the prevalence of HCV seropositivity in our study as done by ***el -Nanawy et al., (1995),*** who reported that the prevalence rate of HCV seropositivity was 44% in thalassemic children and by ***Ni et al.,(1996),*** was 43%.

Ebeling et al.,(1990), reported that rate of anti-HCV seroprevalence among chronically transfused individuals ranging from 41-87%,but with *Weber et al.,(1995)* 18.4% were seropositive for HCV infection. In Britain, *Wonk et al.,(1990)* found 23.2% of thalassemic children were seropositive for HCV infection, but in Switzerland 0.3% *(Grobe and Joller 1990)* .HCV antibody in patients with thalassemia in the united states was 15% *(Kostaridou, 1993)*,but was 1.4% in previous report by *Stevens et al.,(1990)* and in Greec was 29% *(Kostaridou et al.,1993)*,and in Japan 4.3% *(Wantanabe et al., 1991)*.

From the present study, the prolonged duration of illness, the more risk for HCV infection, this denote us that the more units of blood transfusions i.e. the more risks for exposure for HCV infection (54.5% of HCV occurred above age of 12 years).

The increase incidence of contracting of HCV is most probably due to HCV infection is hyperendemic in prevalence in Egypt in comparison to very low prevalence in other countries *(el-Nanawy et al.,1995)*.

So, recently, donor screening for the presence of antibody to the HCV using a first generation test has dramatically reduced the risk of transfusion-associated hepatitis *(Gonzales et al.,1995)* and by second generation anti-HCV provided a significant benefit compared with the first-generation assay*(Takano et al., 1996)*.

HBV infection is common in poly-transfused thalassemic patients all over the world and was serious world-wide health problem ***(Redeker, 1975),*** and chronically infects more than 300 millions persons world wide, ***(lLee, 1991).*** In Egypt 86.6% of polytransfused patients were positive for any of HBV markers ***(El Marsafy 1981),*** also the same with ***Abou Zeid (1989),*** but this percentage was higher being 90% by ***El Shafie (1990).*** This was agreed with the present study, where 89% of cases of multi-transfused thalassemic patients had at least one marker for HBV infection, this high percentage of HBV infection in younger Patient > 7 years old and decreased in < 7 years old due to spread of HB vaccination which gives more protection against HBV infection.

In the present study, subjects were classified depending on the pattern of HBV markers, 11% of the patients had no serologic evidence of exposure to HBV, which may be explained by being either not exposed to HBV contaminated blood units or may have been infected in the past with HBV but lost markers of HBV infection or were genetically resistant to this infection.

This w agreed with ***El Alfy et al.,(1997),*** where on study over 135 polytransfused thalassemic children ,10.4% of them had no marker for HBV, and with ***El Shafie (1990),*** where population of his patients was in younger age. But was contrast to ***El Alfy and Kamel (1994),*** who reported that 38% of his cases had no serologic evidence of exposure to HBV and also as ***El Marsafy (1981),*** who reported that 31.6% of multi-transfused

cases where negative for any of the markers for HBV infection .But ***Abou Zeid (1989),*** found that 3.4% had no any marker for HBV infection in his study.

Screening donors for serological markers of HBV infection by using high-titter anti-HBc screening for donor, the incidence of post-transfusion HB decreased to 0% ***(Takano et al.,1996).***

HCV seropositivity was evenly distributed across the different HBV serogroups but 79% were HBV + HCV infection, this result was in agreement with study done by ***El Alfy et al., (1997),*** where 79.2% of his thalassemic children in his study were seropositive for HBV + HCV infection .

This high percentage in our study may be due to the long duration of illness and so the long duration of blood transfusion.

In our study, 5% of thalassemic patients were ***HBsAg*** seropositive which may denote active infection or carrier state.
This in agreement with ***El Marsafy et al., (1981),*** (7.9%).

But this percentage was lower than previous studies as with ***Saad (1992),*** who reported that in multi-transfused children 44% had hepatitis B surface antigenemia, and by ***El Alfy et al.,(1997),***was 23.1% on study over 135 thalassemic children. By ***Khalifa et al., (1991),*** was 13.2% , ***Kamal (1982),*** was16.6% and ***Abdel Ghaffar (1983),*** was15.7%. ***Essawy et al.,***

(1987), reported that the prevalence of HBsAg among Egyptian infants and children 10.9%.This higher incidence of HBsAg seropositive cases in previous studies may be due to higher prevalence of HBsAg in Egypt. But lower percentage in our study may be due to induction of national program for routine HB vaccination.

100% of HBsAg seropositive cases in the present study had HCV antibodies which is in contrast to a study conducted before in ***(1994),*** by ***El Alfy and Kamel,*** which is 75% and by ***Khalifa et al., (1993),*** which is 25%. This higher incidence of HCV antibodies with HB surface antigenemia is a false impression because HBsAg seronegative had high prevalence of HCV seropositive antibody.

HBcAb (total) was the only marker for HBV infection in 5% of our cases, which may denote active HBV infection with failure of HBsAg expression but 61% of our cases were positive for HBcAb and this is in contrast to the previous study which was done by ***Saad (1992),***where 34% had positive HBcAb. But 88.5%(54/61) of HBcAb cases were HCV antibodies seropositive.

From the present study, according to the age of subjects, 44.9% of HBV infection(40/89) occurred >12 years old, this was in agreement with HCV antibodies where the more risk for viral hepatitis and was significantly associated with increased duration of illness and the volume and number of transfusions.

HBsAb was done for all cases, and found that 46% of cases are seropositive for HBsAb and there is no significant difference between seropositive cases and control. HBsAb seropositive means high rate of immunity or evidence of past HBV infection.

Only 2% of our cases were seronegative for both HBV and HCV infection, their age were 3 years and 4 years and received <50 units of blood, so they benefit from being less exposure for transfusion. This result was in agreement of previous study done by ***El Alfy and Kamel, (1994).***

We select one of the most sensitive liver function of surrogate marker to detect chronic liver disease, ***ALT*** which was determined as a measure of liver cell damage, in our thalassemic group, ALT was highly significant among patients than control. This was in agreement with other studies, where it showed significant increase in all thalassemic groups as with ***El Alfy et al., (1997) Bhatti et al., (1995), el-Nanawy et al., (1995), (Khalifa et al., 1991), Gangemi et al., (1985), Khalifa et al., (1984).*** All these studies, showed that hepatocyte damage with ALT release occurred towards higher value in confirmed positive cases of HCV antibodies and combined HCV + HBV.

ALT level more than two folds than normal was found in 11% of cases. But ALT level less than two folds than normal was found in 24% of cases, with more in combined HBV + HCV subjects, but most of subjects (63%) had normal level of ALT in their sera.

So, ALT level was significantly higher among HCV antibodies seropositive cases than seronegative HCV antibodies group as reported by ***Ni et al., (1996)*** who found that viral hepatitis infection may elevate ALT level. This was in agreement with ***Khalifa et al., (1993),*** that the mean ALT level of HCV seropositive individual was higher than for seronegative ones. In HBsAg, HBsAb and HBcAb, there is no significant difference between seropositive cases and seronegative one.

As regards Hemophilia's

Hibbs et al., (1993), showed a higher seroprevalence of anti-HCV in children with hematopoietic diseases receiving multiple transfusions. Multiple transfused children with evidence of HCV infection had a significantly higher mean number of transfusions when blood products and blood were factored together ***(Khalifa et al., 1993).***Chronically transfused individuals are frequently infected with HCV ***(Abdel Kader and Baliastreri,1993).***

A study population of 10 cases of hemophilic children aged 6-14 years with a mean of 10.4 ± 2.4 was assembled to determine the prevalence of viral hepatitis B and C ,we found that the prevalence of HCV was 80% (8/10) which was in agreement with ***Weber et al., (1995),*** who reported that 87% of hemophiliacs were seropositive for HCV infection by a second - generation ELISA., and ***Khalifa et al., (1993),***reported that 83% of Egyptian children with hemophilia were seropositive for HCV infection and

was similar to that reported from Taiwan (90%), Japan (89%) ***(Isobe et al.,1995), (Schramm et al., 1989),*** Sweden (87%) ***(Chen et al., 1990),***Germany (80%) ***(Widell et al., 1991)*** and in Britain was 76.3% ***(Brettler et al., 1990).***And with ***Kuzin et al., (1996)*** found that 98% of his hemophilic cases had HCV seropositivity and also by ***Lguchi and Ueda (1996)*** , reported that 96.9% of their hemophilic cases had HCV antibodies in their sera.

Frequent transfusion of domestic and /or imported coagulation factor concentrates probably caused the high incidence of HCV infection ***(Tagariello et al., 1995)***.

But this result is in contrast with ***Polz et al., (1995),***where they found that 59% of their hemophilic patients had HCV antibodies in their sera, and ***Montes et al., (1995)*** whom reported that HCV was represented a prevalence of 30% in there hemophilic patients.

The prevalence of HBV infection among hemophiliacs was 80% (8/10), this result is in contrast to that reported by ***Kuzin et al., (1996),*** whom found that 97% of their hemophilic cases were infected with HBV.

This higher percentage due to prolonged duration of illness among the patients, clearly ,the number of transfusions required is more likely to increase with the length of illness, these data are further strengthened by the finding of parallel between increased prevalence and increased volume and number of blood only and blood products transfusion ***(Montes et al.,***

*1995)*and induction of national program for routine HB vaccination was not present before.

There is only one case (1/10,10%) of the hemophilic cases had no any marker for HBV or HCV infection, this is may be due to short duration of illness or due to good screening for donors for HBV or HCV.

All cases were seronegative HBs antigenemia, but 4 cases (4/10,40%) had seropositive for HBsAb and also the same number had HBcAb seropositive.

As regards to ALT level, there is highly significance between cases and control.

SUMMARY AND CONCLUSION

The aim of this work is to study the incidence of HB and HC infection among multi-transfused pediatric patients.

The study comprised of 110 multi-transfused children ,100 thalassemics (66 males, 34 females) ranged between 3-15 years with mean (11.1 ± 3.3) and 10 hemophiliacs (all are males) aged 6-14 years with mean (10.4±2.4) and 20 healthy children (15 males, 5 females) ranged 5-14 years with mean (9.6 ± 2.6), they served as control group.

All cases and control groups were subjected to full history, clinical examination and serological markers of hepatitis (HBsAg, HBsAb, HBcAb (IgG)) and HCV antibodies by ELISA technique and determination of ALT enzyme by colorimetric. Ultrasonography was done for all cases.

The results of this study as for thalassemic children showed that the incidence of hepatitis markers reactivity, the highest incidence was combined HBV + HCV infection (79 %), then HBV only (10%) then HCV antibodies only (9 %) and only 2 % had no any marker for HBV or HCV infection.

As regards for hemophiliac patients ,the hepatitis markers reactivity, the combined HBV + HCV infection was the highest (70 %), then HBV only (10%) and HCV antibodies only (10 %) and 10 %of these patients had no any marker for HBV or HCV infection.

Comparison of the level of ALT among control and multi-transfused children ,showed that among thalassemics ,the mean [45.3±39.51] and for hemophiliacs [46.7±27.95] which showed significance difference than control [8.5 ±4.01].

And by ultrasonography for all cases of thalassemic patients showed that all cases had hepatomegaly but no cirrhotic changes and 88 patients had no spleen [splenectomized] and the other 12 patients had splenomegaly.

Previous studies found that patients with history of multi-transfusion, the median time between blood transfusion and the diagnosis of cirrhosis was 24 years.

So, we concluded in our study that the more the units of blood transfusion the more numbers of patients were catching hepatitis infection [B or C or both].

RECOMMENDATION

After finishing of this study, we recommended that :-

- *1) Must do secreening for all blood donors for decreasing possibility of transfused hepatitis infection to multi-transfused patients.*
- *2) Multi-transfused patients whom are free from hepatitis B infection must be vaccinated by HB vaccine and before the1st. blood transfusion .*
- *3) Thalassemic patients must by iron chelating well to prevent iron over load which enhances viral hepatitis infection.*
- *4) Must do PCR for every patient who is seropositive for HCV antibodies.*

5) Must follow up of multi-transfused patient specially with long standing infection with HBV or HCV for detection of liver cirrhosis or early detection of HCC by regular ultrasound to the liver, liver biopsy for histopathology and ALT enzyme in his serum.

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