Abstract:

Background: Type-1 diabetes is one of the largest endocrine and metabolic health issues among children and young adults. Diabetes mellitus is associated with many long-term complications. Aim and Objectives: To compare outcomes in groups monitored either by real time continuous glucose monitoring or by Self Monitoring of Blood Glucose (SMBG; 3-4 blood glucose measurements per day). Also we studied barrier for the use of CMG. Material and Methods: It is a prospective quasi experimental controlled trial at diabetic center in Abha, KSA. Out of 307 patients registered, 60 T1DM patients agreed to participate; out of them 30 patients were enrolled in intervention cohort, they used CGM sensor continuously while 30 patients were in the control group they used SMBG. All were followed for 6 months; HbA1c was measured at 3 and 6 months. Barrier to use of sensor was evaluated with a questionnaire. Results: At baseline no significant difference was observed in the average HbA1c between the groups (10.57 % vs 10.73 %). HbA1c reduction compared to baseline levels in the intervention cohort was 2.15% and 2.36% at 3 and 6 months. In control group, HbA1c reduced to 1.07% and 1.22% at 3 and 6 months showing significant difference (p=0.002 and p=0.001 at 3 and 6 months). Younger patients age <20 years had significantly better reduction of HbA1c (2.28% vs 1.27%, p=0.015 and 2.47% vs 1.98%, p=0.004 at 3 and 6 months). The hypoglycemic events were statistically reduced in the intervention group (p<0.001) and also the ketoacidosis and hospital admissions (20.0% vs 3.3%, p<0.001). Conclusion: We found that the use of CGM sensor was associated with significant HbA1c reductions and improved glycaemic control.

Keywords: Type-1 diabetes, Hemoglobin A1c, Hypoglycemia, Continuous Glucose Monitoring, Self Blood Glucose Monitoring

Introduction:

Type-1 diabetes is one of the largest endocrine and metabolic health issues among children and young adults [1]. Globally an estimated 542,000 children are living with type-1 diabetes and this disease is increasing by 86,000 new cases each year with an annual incidence of 3%. Saudi Arabia is among the top ten countries for increasing numbers of this condition with an incidence of 31.4/100,000; as reported in the latest Diabetes Atlas [2]. Epidemiological studies [3, 4] reveal that patients with type-1 diabetes have abridged life expectancy and higher morbidity due to multiple acute and chronic complications. A study from Scotland documents the reduction of subsequent life expectancy at age 20 years of approximately 11 years for men and 13 years for women compared with the general population without the disease [3]. Diabetes mellitus is associated with many long-term complications. These are categorized into two types; micro-vascular complications that affects eyes, kidney, peripheral and autonomic nervous system and macro-vascular complications that affect cardiovascular system [4].
A strong association has been documented between the level of glycaemic control and the incidence and amelioration of these diabetic complications [5]. The Diabetes Control and Complications Trial (DCCT) I and its long-term observational follow-up, the Diabetes Interventions and Complications (DCCT/EDIC) study during their many years of follow-up, provided unquestionable evidence of a very close, curvilinear relation between the degree of glycaemic control (measured by hemoglobin (HbA1c) concentrations), maintained over the long term, and the onset or progression of micro-vascular and likely also macro-vascular complications [6]. Hence tight glycaemic control with intensive insulin therapy has been the best evidence based strategy to face these challenges.

In light of such evidences the overall recent recommendation has suggested the goal for HbA1c to be achieved as close to normal blood glucose and HbA1c levels as possible [7] but despite prodigious efforts, the ability to reach normal HbA1c levels is hampered by the limiting occurrence of hypoglycemia and the risks related to the problems associated with hypoglycemia, which are increased if meticulous glycaemic control is sought. Hypoglycemia is considered the greatest impediment to strict glycaemic control [8] and the fear of hypoglycemia often leads patients to forget the fatal consequences of long-term complications resulting in loss of control and hyperglycemia [9]. With the recent availability of newer technologies to monitor continuous glucose monitoring these adverse effects can possibly be offset by adjusting the doses of insulin according to the need.

Compared with conventional intensified glucose monitoring, defined as three to four blood glucose measurements per day, continuous monitoring provides much greater insight into glucose levels throughout the day. This technique of monitoring uses a wire-type glucose sensor that is implanted in the subcutaneous tissue to monitor the interstitial fluid glucose concentration of diabetic patients; although it does not puncture any blood vessels it reflects the patient's blood glucose levels. Continuous glucose monitoring provides information on direction, magnitude, frequency, and duration of glycaemic oscillations on a moment to moment basis to aid control of diabetes by patient himself and can help identify and prevent unwanted periods of hypo- and hyperglycemia [10, 11].

However despite the documented attractive, beneficial effects for Continuous Glucose Monitoring (CGM) in studies; the full clinical potential impact of CGM is far from being realized and many physicians still feel reluctant to get abide by this new technology and prefer the conventional glucose monitoring due to lack of experience and due to few controversy in literature related to CGM use [12-14]; some meta-analyses of studies showed that CGM use was not superior to Self-Monitoring of Blood Glucose (SMBG) with regard to metabolic control among pediatric patients with T1D [12, 13]. Similar results were also reported from the 2008 landmark Juvenile Diabetes Research Foundation CGM randomized controlled trial, in which overall blood glucose control in children age 8–17 years old assigned to the CGM group did not differ from the SMBG group [14].

The other major issues and barrier to using the sensor CGM has been documented to be; greater time consumption as patients have to constantly focus on diabetes care [15], calibration, training
and education of patients and cost of the sensor [16].

The aim of the present study, therefore, is to analyze the improvement in glycaemic control and effectiveness in preventing hypoglycemia with the use of CGM and to identify the barrier associated with routine clinical use of such technology.

**Material and Methods:**

**Study design:**

This study was a prospective quasi experimental controlled trial comparing outcomes of treatment for T1DM with intensive insulin therapy; monitored either by real time CGM or by SMBG in the two groups.

**Setting and Participants:**

The study was carried out from January 2016 to June 2016 at diabetic center in Abha, Aseer region of Saudi Arabia. The center is associated with the only tertiary care unit in this region. All diagnosed type-1 diabetic patients are referred to this center from different hospitals and Primary Health Care Centers (PHCCs) in this region.

A separate team was identified to supervise the intervention trial for this study. The team included; one consultant diabetologist, nurse, pharmacist who was expert in the technique of using the sensor and an emergency medical officer. Three days training was given to the team about the trial by the consultant diabetologist. The study enrolled patients with type-1 diabetes aged 3 to 29 years, who agreed to wear a continuous glucose monitor and to give a written informed consent for this. Exclusion criteria were limited to severe medical or psychological co-morbidity.

All 307 T1DM patients who were registered in the diabetic clinic of Abha during the year 2015 were approached to be included in this study. Out of these, sixty T1DM patients agreed and volunteered to participate. These patients were assigned in two groups; 30 patients were included in the intervention cohort while 30 patients were included in the control. Preference allocation was used to make intervention and control groups. Patients or parents who preferred to use CGM were included in the intervention group while those who preferred to use SMBG comprised control group.

Base line HbA1c level was measured from both intervention and control group before intervention. The participants were followed prospectively for six months; HbA1c was measured at three months and later at six months. Patients were contacted and a reminder was given over telephone at least 3 days before the date of each follow up for reviewing glucose data and to adjust diabetes management.

**Study device:**

Dexcom CGM sensor was used for the study. The sensor continuously displayed real-time interstitial glucose values and was calibrated prospectively using SMBG reference values. High/low alert thresholds were set at 50–70 mg/dl for hypoglycemia and 170–250 mg/dl for hyperglycemia. The upper alarm was later reduced to 200 mg/dl after the first 10 days. Settings were readjusted during the study when required by the expert at the clinic.

**Study Protocol:**

Prior to the commencement of the study, all subjects and parents in the CMG using group were given intense training for 3-7 days by the team at the clinic for the usage of device, this included; inserting and calibrating subcutaneous sensors, operating the continuous monitoring device, and
to check readings for the sugar levels. Also they were trained for modification of insulin doses according to the results. The sensor was worn on abdomen and the subjects used the RT-CGM system for 7 days, to achieve continuous RT-CGM glucose values.

Both the groups were having same type of insulin therapy including; Lantus and Novorapid by multiple injection technique. All patients were encouraged to maintain their blood glucose concentration within the preprandial target range of 70 to 130 mg/dL and with peak postprandial values below 180 mg/dL. The patients with CMG sensor made changes in the dose of therapy according to the written instructions provided and explained to all the subjects. Patients were instructed to perform confirmatory SMBG measurements before therapeutical interventions or corrective action if hypo- or hyperglycemic alarms or symptoms occurred.

**Hypoglycemia:**
It was defined as mild when the sugar levels were below 70 mg/dl as defined by American Diabetic Association (ADA) [17], report published in 2005 and the patients were trained to be able to self-treat themselves, according to written instruction. While it was considered as severe hypoglycemia when there was need for external help and hospital admission [18].

**Diabetic ketoacidosis:**
This was diagnosed with patient's plasma glucose concentration above 250 mg per dL, pH level less than 7.30, and the bicarbonate level 18 mEq per L or less, serum ketones and presence of Beta-hydroxybutyrate in urine [19].

**Follow-up:**
All patients were asked to visit 2-3 days after starting the study to check upload of all devices and to confirm that continuous data were recorded appropriately. Further visits were conducted at one month, three months and six months. At each visit data were uploaded for all the patients in both groups and were inquired for any symptoms if present, about adverse events including hypoglycemia, hyperglycemia, device-related or study-related untoward events and also for patients' satisfaction. They were examined clinically for any complication and investigations were done at 3 months and 6 months; including blood sugar levels, HbA1c, blood urea, creatinine, electrolytes and urine detailed report from a central laboratory at the Diabetic Center. At each visit, any adverse and serious adverse events regardless of cause were reviewed and reported.

**Barrier to Use:**
We developed a short questionnaire to discover the obstacle/obstacles that patients considered to be a problem in continuing CGM in their future life. This questionnaire addressed the issues like; cost, time consumption, calibrations, cumbersome interpretation, difficulty in approaching the expert, lack of satisfaction and difficulty in using it.

**Outcome Measure:**
The primary outcome was the change in the mean HbA1c level from baseline to six months. Secondary outcome was to find out difference of occurrence of hypoglycemia, Diabetic Ketoacidosis (DKA) and admission in hospital in the two groups. The third outcome measure was to identify the barriers to use of CGM.

**Statistical analysis:**
The data was analyzed by SPSS and PC version 20.0. To compare the baseline characteristics of the participants Fisher exact tests was use for
categorical variables and t tests for continuous variables. For comparing the difference of HbA1c in intervention and control group, we used t tests. The statistical significance set at 5%.

**Results:**
A total of 60 participants were included in this study. No participants were lost to follow up in the study groups. Mean age of the participants was 11.6±6.1 years. No significant difference in mean age between intervention and control group was observed; mean age of intervention group was 12.8±7.8 years and control group 10.9±3.4 years. The education level of fathers in the intervention group was significantly higher compared to the control group (Table 1).

Table 2 shows the difference of HbA1c level in intervention and control. At baseline no significant difference was observed in the average HbA1c level between intervention and control group (10.57 % Vs 10.73 %) however the intervention group had a significantly low level of HbA1c at 3 months (p=0.002) and 6 months (p=0.001) of intervention compared to the control group.

Figure 1 illustrates the relative reduction in HbA1C levels from baseline for the intervention and control group. A one way repeated measured analysis of variance (ANOVA) determined that mean concentration of HbA1c differed significantly between time points $F (49.874, p<0.001)$. HbA1c concentrations decreased significantly in both the groups with the CGMS (from 10.57% to 8.42%, $p<0.001$) at 3 month and (from 10.57% to 8.21%, $p<0.001$) at 6 months while in the control group (from 10.73 to 9.66, $p = 0.053$) at 3 months and (from 10.73% to 9.51, $p=0.05$) at 6 months. The intervention group displayed significantly the greatest fall in HbA1c levels. In the intervention group HbA1c decreased 2.15 % at 3 months and 2.36 % at 6 months from base line while in control group HbA1c fall only 0.91 % at 3 months and 1.22 % at 6 months from base line. Follow up comparisons in intervention group indicate that each pair wise difference was significant $p<0.001$. There was significant decrease in level of HbA1c over time suggesting that the CGM user have significant reduction of HbA1c level.

The intervention group reported no episodes of hypoglycemia during the 6-month study period. Conversely the control group reported 13 (43.3%) hypoglycemic events. This difference in occurrence of hypoglycemia between the two groups was statistically significant ($p<0.001$). (Table 3). Amongst the patients who suffered a hypoglycemia in the control group four patients had a single episode, four patients had two episode, two patients had three episodes and three patients experienced 4 hypoglycemic episodes. More than half of the patients in the control group (53.8%) developed severe hypoglycemia, two to three times and 6 (43.3%) of the control group needed a hospital admission. In addition a significant number of patients developed diabetic-keto acidosis and needed to be admitted to hospital in the control group, compared to the intervention group (20.0% vs, 3.3%, $p < 0.001$).

On analysis of patient demographics in the intervention and control groups at 3 and 6 month intervals, no demographic factors showed a significant difference of mean level of HbA1c (data not shown). Analysis of demographics factors with the intervention group at 3 and 6 month interval from base line reveals that only age has a significant relation with reduction of HbA1c level with more reduction of HbA1c level in younger age group compared to older age group.
The patient with age group below 20 years, HbA1c level reduced 2.28% while patients with age group 20 years and more, HbA1c has reduced 1.68% from baseline after 3 months (p=0.015). Similarly at six months from baseline it has reduced 2.47% amongst the patient age group below 20 years and 1.98% (p=0.004) amongst the patients 20 years and above (Fig. 2).

Our study investigated how continuous glucose monitoring affected patients and families in everyday life. Continuous glucose monitors received positive feedback from patients and their families and stated that, they were glad that patients in the intervention group did not have any hypoglycemia. We also explored the barriers of use of CGM on cost of machine, calibration of machine, reading the data and time consume. Only cost was reported a barrier about 14 (46.7%) of the patients in use of CGM (data not shown).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Intervention group</th>
<th>Control group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 10 years</td>
<td>16 (53.4%)</td>
<td>18 (60.0%)</td>
<td>0.064</td>
</tr>
<tr>
<td>11-19 years</td>
<td>7 (23.3%)</td>
<td>7 (23.9%)</td>
<td></td>
</tr>
<tr>
<td>≥ 20 years</td>
<td>7 (23.3%)</td>
<td>1 (3.3%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13 (43.3%)</td>
<td>13 (43.3%)</td>
<td>0.063</td>
</tr>
<tr>
<td>Female</td>
<td>17 (56.7%)</td>
<td>17 (56.7%)</td>
<td></td>
</tr>
<tr>
<td>Father education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to Secondary level</td>
<td>8 (26.7%)</td>
<td>20 (66.7%)</td>
<td>0.003</td>
</tr>
<tr>
<td>College &amp; university</td>
<td>22(73.3%)</td>
<td>10 (33.3%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HbA1c Level</th>
<th>Intervention group Mean ± SD</th>
<th>Control group Mean ± SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base line</td>
<td>10.57±1.69</td>
<td>10.73±1.62</td>
<td>0.435</td>
</tr>
<tr>
<td>After 3 months of intervention</td>
<td>8.42±1.2</td>
<td>9.66±1.6</td>
<td>0.002</td>
</tr>
<tr>
<td>After 6 months of intervention</td>
<td>8.21±1.1</td>
<td>9.51±1.7</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Table 3: Comparison of Occurrence of Events between Intervention and Control Groups

<table>
<thead>
<tr>
<th>Events during trial</th>
<th>Intervention group</th>
<th>Control group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>30 (100.0%)</td>
<td>17 (56.7%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>--</td>
<td>13 (43.3%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Severe hypoglycemia</td>
<td>--</td>
<td>7 (53.8%)</td>
<td></td>
</tr>
<tr>
<td>Mild hypoglycemia</td>
<td>--</td>
<td>6 (46.2%)</td>
<td></td>
</tr>
<tr>
<td>Diabetic Ketoacidosis (DKA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 (3.3%)</td>
<td>6 (20.0%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No</td>
<td>29 (96.7%)</td>
<td>24 (80.0%)</td>
<td></td>
</tr>
<tr>
<td>Admission due to DKA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 (3.3%)</td>
<td>6 (43.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td>No</td>
<td>29 (96.7%)</td>
<td>24 (56.7%)</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1: Improvement of HbA1c Level in Intervention and Control Groups at 3 Months and 6 Months
Discussion:
This interventional study is among the initial few studies in the Kingdom of Saudi Arabia to demonstrate the effectiveness of CGM sensors on the glycaemic control and on preventing extreme levels of blood sugar. The education level of fathers of the patients in the intervention group was higher compared to the control group; this reflected the interest and enthusiasm in not only using the new technique and agreeing to participate in the intervention group but also in following all the instructions meticulously. This has been mentioned in previous literature that education and interest are important factors that promote the use of CMG [10, 20]. Although both the groups had equally uncontrolled sugar at baseline the intervention group had significant improvement in glycaemic control over 6-months period in comparison to the control group; this finding is similar to multiple other studies that also revealed the same fact that there is significant role of using CGM in improving the glycaemic control reflected by reduced HbA1c blood levels in patients with type-1 diabetes [11, 21-23]. However, all the studies do not show similar reduction and the reduction values vary; for example after completion of a 6-month randomized controlled trial one study reported significant reduction in HbA1c of 0.4% [21]. One other study documented the reduction of HbA1c concentration of 0.2% [22]. One nonrandomized, uncontrolled trial with 28 type-1 diabetic subjects, HbA1c was documented to reduce by 0.40 and 0.43% at 3 and 6 months, respectively [24]. A study using CMG to find glycaemic control in patients with poorly

Fig. 2: Age Specific HbA1c level in Intervention Group

![Graph showing Age Specific HbA1c level in Intervention Group](image)
controlled type 1 diabetes only; documented that its use gradually improved glycaemic control over 3 months, resulting in a reduction in A1C by at least 1% in half of their patients and at least 2% in one-quarter [25]. This difference of greater reduction of HbA1c levels in our study may be due the fact that our subjects used the sensor continuously that is for greater than 86% of time, while in most of other studies mentioned used the device for shorter time period and the time interval differed in these studies. In contrast to our finding, few prior studies documented that with using CMG there was no significant difference in glycaemic control [26-28] for example a meta-analysis found that; compared with SBGM, CGM was associated with a non-significant reduction in HBA1c (0.22%; 95% CI: −0.439% to 0.004%, p = 0.055) [26]. Similar to this another study documented that the differences in HbA1c between groups was there but did not reach statistical significance (p=0.13) [27]. A randomized controlled trial of CGM in those aged 4–9 years for 26 weeks showed use of CGM (>6 days per week) did not correlate with improvement of HbA1c. The authors explained that this may have been due to parent's fear of hypoglycemia that retrained them for more aggressive insulin changes [29].

Our study revealed that the benefit of using the sensor for CGM in the younger age group (<20 years) had significantly better reduction of HbA1c at 3 months and 6 months compared to patients older to this age; This outcome is in contrast to some previous studies; [14, 21, 23] where it was found that the sensor was more useful in type-1 diabetic patients belonging to higher age group but these studies at the same time documented that the observed age effect may be related to substantially greater use of sensors in the adults than in patients in the younger groups. However our results must be interpreted with caution since the patient fathers were highly educated in our intervention group with most of them having postgraduate degrees and their families were also highly motivated as a result the younger patients under their care reported better results.

The intervention group in our study shows significant difference in episodes of any mild or severe hypoglycemia in compared to the control group; such a finding of reduced frequencies of hypoglycemia and shorter time spent in hypoglycemic range have been demonstrated in many studies [30-33]. A study assessing the impact of CMG on hypoglycemia in people with type 1 diabetes documented that the time per day spent in hypoglycemia was significantly shorter in the continuous monitoring group than in the control group (0.48 ± 0.57) and (0.97 ± 1.55) h/day [30]. Another study that evaluated the effect of CGM on the frequency of severe hypoglycemia also documented that; over a 1-year follow-up period, the median rates of severe hypoglycemia were reduced from 4.0 (Interquartile Range [IQR] 0.75–7.25) episodes/patient-year to 0.0 (0.0–1.25) episodes/patient-year (p < 0.001), and rates were reduced (from 8.1 ± 1.3 to 0.6 ± 1.2) episodes/year (p = 0.005) [34]. A 6-month trial (IMPACT) in well controlled type-1 patients documented that the hypoglycemia (<70mg/dL) in the CGM group declined by 38% from 3.38 to 2.03 hours/day [35]. However in contrast to our finding some studies documented no significant difference in the number of hypoglycemia episodes or severe hypoglycemia between the groups [14, 23, 26]; for example in a study by Juvenile Diabetes Research Foundation it was documented that in the intervention group with patients using CMG; the time spent in the hypoglycemic range of <70
mg/dL was reduced by 41%, compared to the control group who had no change, however, there was no significant difference in the number of hypoglycemia episodes between the two groups and this was explained by the fact that in their study, CGM sensor use was dropped from 78% of the time in the first 4 weeks to 67% in the final 4 weeks and this may be the reason for this result [36]. Similarly in one other study it was found that the rate of severe hypoglycemia was low but did not differ between the two study groups significantly; however they admitted that the trial was not powered to detect such a difference [14].

In addition our study revealed that in intervention group there was a significant decrease in number of patients who developed diabetic- ketoacidosis and hospital admission due to any of the severe adverse problem compared to control group. This could be due to the reduced duration of hyperglycemia (min/day blood sugar $\geq 240$ mg/dl) as also mentioned in a meta-analysis [23] along with better planning of daily and supplemental insulin doses, ability to take preventive action for rising and falling blood sugar levels, and avoidance of factors that may negatively affect glycaemic control [21].

All the patients in the intervention group were found to be very satisfied with the CGM sensor and were confident that they may now control their blood sugar level without experiencing the complication of hypoglycemia; they were highly motivated to use it in future and the only barrier to use by 46% of patients was the cost of the sensor. This is in accordance to a study that found that if patients have the option to self-fund these sensors, they remain quite expensive [31].

**Conclusion:**

Our study strongly documents that CGM, offers a valuable therapeutic option for the management of type-1 diabetes and provides further efficacy and safety benefits beyond SMBG. We found that the use of CGM sensor is associated with clinically significant HbA1c reductions and improved glycaemic control. Also it appears to be a useful clinical tool that helps in preventing blood sugar excursions. We found reduced episodes of diabetic ketoacidosis and significantly reduced episodes of hypoglycemia.

Considering expenses associated with both complications and social factors of type-1 diabetes the cost of sensor although more still shows to be a feasible tool to manage young diabetic patients; especially for affording patients and for patients who are not able to achieve target glycaemic control with conventional therapy or when experiencing problematic hypoglycemia.

**Limitation of the Study:**
The limitation of our study was the relatively shorter time period for the study. Extending the same study to future may reveal more confirmatory data. Also proper randomization and complete removal of the element of bias by appropriate blinding was not practically possible.

**Acknowledgement:**
We would like to extend our thanks to Dr Helmi Ahmed, Dr Osamah Basomid, Nurse Alfira, Nurse Diwa and all members of the team appointed for the study at the diabetic clinic for educating the patients, sensor application, calibrations, collecting the data and for extending their kind support and cooperation to make this study possible. Also we would like to thank Prof Shamsun Nahar for her expert advices related to analysis and writing the results.
References


*Author for Correspondence:* Dr. Hassan M. Al-Musa, Family and Community Medicine, Department College of Medicine, King Khalid University, P.O. Box 641, Abha, K.S.A Contact: 0501882929 Email: fcmcomkku@gmail.com, almusa3@hotmail.com