REVIEW OF LITERATURE

The study of place of magnesium in medicine is further complicated by the fact that its requirement in the body is influenced by a number of factors. During periods of rapid formation of new tissues the magnesium requirement goes up. Conditions that interfere with magnesium absorption or enhance its urinary excretion, increase magnesium requirement. High intake of calcium, phosphates, proteins and vitamin D increases the magnesium requirements.

With so many factors influencing the absorption and excretion of this element, and also the amount needed for metabolic processes, it remains a controversial question as to what the normal magnesium requirement is? There is probably no uniform optimal need. To determine the magnesium status it is necessary to establish the normal values. So that diagnosis of even subacute or long term magnesium deficit may be made easily and the adequacy of response to supplements may be judged.

There is so great a variation in the normal values of serum magnesium cited by different authors that it is difficult to call what is normal. The main thing that
is responsible for these various is that different authors have used different methods of determining the serum magnesium in normal persons. Some authors have used hospital patients as normal subjects, which could have been the cause of this discrepancy. There is evidence that the physiochemical state of the magnesium in the serum may deviate from normal in several conditions associated with magnesium deficit. (Bajpai et al 1967, Gitelman et al 1969, Silverman et al 1954).

Serum Magnesium levels in normal subjects (Non pregnant):

Plass and Bogart (1933) were amongst the earliest workers to report on the magnesium content of blood in human beings. In their series of healthy woman the average values of serum magnesium were found to be 2.3 mg%. Becher and Bomskov (Both 1932 individually) found the range of serum magnesium in normal healthy individuals as 1.8 to 2.3 mg% and 1.7 to 2.6 mg% respectively.

Wacker and Fahrig (1932) reported this value to be 2.40 mg%. A little higher values for serum magnesium were reported by Greenberg et al (1933) who found these to be from 2.0 to 3.6 mg%, the mean being 2.74 mg%. 
Shohi (1933) set the limits from 1 to 3 mg% which were more in accordance with those of Becher and Bomskov noted above.

Walker and Walker (1936) used 87 students of medical college for estimation of normal serum magnesium values. Their values ranges from 1.6 to 3.0 mg% the mean being 2.2 mg%. These values also approximated those of Becher and Bomskov as given above.

Velluz and Velluz (1934), Cope (1936) and Brookfield (1937) reported same. What similar values for serum magnesium in their normal female individuals. Their mean values were 2.00, 2.06 and 2.04 mg% respectively. Wolf (1936), Hoffman (1937) and Raices (1938), noted higher values in their cases which were 3.61, 2.16 and 2.44 mg% respectively. Bernstein and Simkins (1940) recorded 2.13 mg% as the mean value of serum magnesium in their normal female individuals.

Haury (1942) observed that the normal range of serum magnesium in his series was between 1.7 and 3.0 mg%. He also analysed and compared the mean serum magnesium values of various authors and commented that these stood in the vicinity of 2.4 mg%.

Simonsen et al (1947), Orange and Rhein (1951) and Polonowski (1953) reported compromising readings about the serum magnesium. Their findings were 1.9 - 2.4, 1.8- 2.2 and 1.87 mg% respectively.
Andreasen (1957) observed the range of serum magnesium in normal non pregnant women to vary from 1.53 to 2.21 mEq/L with a mean value of 1.87 ± 0.17 mEq/L.

Hall (1957) estimated serum magnesium level in 30 non pregnant women of child bearing age and free from cardiovascular and renal disorders. His mean value was reported to be 1.87 ± 0.20 mEq/L. Haunter (1958) found the mean serum magnesium level to be 1.90 mg% in his normal female cases.

Achari et al (1961) determined serum magnesium levels in 20 normal subjects and reported that the normal serum magnesium in their cases ranged from 1.80 to 3.20 mg% with mean of 2.38 ± 0.35%. The value closely approximated to be found by Haury (1940).

A series of 52 samples of blood from normal healthy individuals was studied by Roychowdhary, Khan, Bose and Habibi (1962) for the estimation of serum magnesium. These workers reported a mean values of 2.32 ± 0.108 mEq/L. This value was higher than those reported by Hall and Hunter but matched with those Haury and Bernstein et al (all noted above).

Laha et al (1963) determined magnesium levels in 100 normal adults and reported that the normal serum magnesium in their cases ranged from 1.73 to 3.00 mg% with a mean
of 2.41 mg% ± 0.34. They employed chemical methods for magnesium estimation.

Goldsmith and Goldsmith (1966), in a series of 17 normal women found serum magnesium fluorometrically to be 1.73 ± 0.15 mEq/L.

In a series of 12 normal subjects analysed by atomic absorption Lida, Fawa and Wacher (1967) gave an average value for serum magnesium of 1.81 ± 0.18 mEq/L.

Jain et al (1969) studied serum magnesium levels by chemical method in renal diseases. Their study included 59 cases of various types of renal disease and results were compared with magnesium levels in serum in 20 normal persons. Their normal values of serum magnesium ranged from 1.54 to 2.80 mg% with a mean of 1.94 mg%.

Bajpai et al (1970), using Titan yellow method, estimated serum magnesium in their control cases. Their values ranged from 1.63 to 2.25 mEq/L, the mean being 1.69 ± 0.16 mEq/L.

Singh et al (1979), using Titan yellow method in 25 non-pregnant cases and a mean value of 2.097 ± 0.056 mg% was reported.
Summary of the serum magnesium reported by some recent authors and the method of estimation employed (in normal subjects)

<table>
<thead>
<tr>
<th>Name of workers</th>
<th>Magnesium concentration in serum</th>
<th>Method employed for estimation</th>
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</thead>
<tbody>
<tr>
<td>Pile et al (1958)</td>
<td>1.65 mEq/L</td>
<td>Chemical</td>
</tr>
<tr>
<td>Montgomery (1960)</td>
<td>1.71 mEq/L</td>
<td>Flame photometry</td>
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<tr>
<td>Rangam et al (1961)</td>
<td>1.68 mg% ± 0.27 (1.33 - 2.5 mg%)</td>
<td>Chemical</td>
</tr>
<tr>
<td>Kalgi (1962)</td>
<td>Males 2.14 mEq/L Females 2.34 mEq/L Children 2.88 mEq/L</td>
<td>Chemical</td>
</tr>
<tr>
<td>Roychowdhary (1962)</td>
<td>2.32 ± 0.108 mEq/L</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Laha et al (1963)</td>
<td>2.41 mg% ± 0.34 (1.73 to 3.09 mg%)</td>
<td>Chemical</td>
</tr>
<tr>
<td>Linder et al (1963)</td>
<td>1.4 to 2.2 mEq/L</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Banerjee et al (1964)</td>
<td>1.6 to 4.3 mg%</td>
<td>Chemical</td>
</tr>
<tr>
<td>Pradhan et al (1964)</td>
<td>1.68 mg% (1.52 to 2.80 mg%)</td>
<td>Chemical</td>
</tr>
<tr>
<td>Radhakrishna (1964)</td>
<td>2.17 mEq/L</td>
<td>Titan yellow</td>
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<tr>
<td>Chhaparwal et al (1966)</td>
<td>2.01 mEq/L</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Zutshi (1966)</td>
<td>1.87 ± 0.63 mEq/L (10 to 2.8 mEq/L)</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Khanna et al (1966)</td>
<td>2.00 mEq/L (1.20 to 2.73 mEq/L)</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Jain et al (1969)</td>
<td>1.94 mg% (1.56 to 2.80 mg%)</td>
<td>Chemical</td>
</tr>
<tr>
<td>Bajpai et al (1970)</td>
<td>1.66 ± 0.16 mEq/L (1.63 to 2.25 mEq/L)</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Pontis et al (1977)</td>
<td>2.080 ± 0.368 mg%</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Sarin et al (1987)</td>
<td>2.25 ± 0.12 mg%</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Singh et al (1979)</td>
<td>2.097 ± 0.056 mg%</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Rizvi et al (1979)</td>
<td>2.68 ± 0.396 mg%</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Khan et al (1987)</td>
<td>2.53 ± 0.30 mg%</td>
<td>Titan yellow</td>
</tr>
<tr>
<td>Verma et al (1989)</td>
<td>2.52 ± 0.28 mg%</td>
<td>Klett Summersen photo electric colorimeter</td>
</tr>
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Rizvi et al (1979), Sarin et al reported serum magnesium levels in their non pregnant cases. Their values were $2.68 \pm 0.39$ mg% and $2.25 \pm 0.12$ mg% respectively.

Khan et al (1989), using Titan yellow method in 10 non pregnant cases and a mean value of $2.53 \pm 0.30$ mg% was reported.

Manju Verma et al (1986), using Klett Summersion photoelectric colorimeter method in 25 non pregnant women and a mean value of $2.52 \pm 0.28$ preovulatory phase and $2.41 \pm 0.29$ ovulatory phase was reported by them.

Pontis et al (1977) measured serum magnesium in 25 normal nonpregnant women and a mean value of $2.080 \pm 0.368$ was reported.

**Serum Magnesium levels in normal pregnant women:**

The earliest available data on the magnesium content of animal or human tissue during pregnancy comes from the work of Sichal, who in 1899 published data concerning the chemical composition of human Embryo and foetus at various stages of pregnancy.

Krebs and Briggs (1923) reported on blood magnesium levels in 17 pregnant women at from 8 - 40 weeks of gestation. The number of sample was too small to permit any
evaluation of changes during pregnancy. But the authors found the magnesium concentration of the blood to vary between 2.1 to 2.7 mg%.

In another study, published in the same year, Plass and Bogert (1923) measured serum magnesium in 40 pregnant women at various stages of pregnancy, and compared their values with those of normal non-pregnant women. Although the serum magnesium level of non-pregnant women appeared to be quite constant with an average value of 2.3 mg%, that of pregnant women fell from an average value of 2.35 mg%, at the beginning of pregnancy to an average of 2.10 mg% at the end of pregnancy.

Wolf et al. (1937) measured serum magnesium in 22 pregnant women between the 2nd and 9th month of pregnancy and found a decrease in the concentration of the element at the beginning of pregnancy, followed by a slight increase. Serum magnesium in early pregnancy was 1.5 to 1.7 mg%.

In a more extensive study, Hall (1957) determined serum magnesium in 294 pregnant women from 11 weeks of gestation to term and in 30 cases at 6 weeks postpartum. As compared with the mean of normal non-pregnant women (1.87 ± 0.29 mEq/L), serum magnesium was depressed during pregnancy, falling as low as (1.6 mEq/L).
Achari et al (1961) measured serum magnesium level in normal pregnant women the value lies between 1.70 to 3.20 mg%, with a mean of 2.41 ± 0.36 mg%. The serum magnesium level approximate vary well with figure obtained with normal subjects. P ≤ 0.8 which indicates that the value of serum magnesium of normal subjects does not significantly differ those of pregnant women.

De-Jorge and his collaborators (1965a) found that serum magnesium levels in 99 pregnant women fell continuously from a level of about 1.6 mEq/L in the 2nd month, to about 1.2 mEq/L in the 8th month, while the normal non pregnant value was 2.00 mEq/L.

Celli Arcella (1966) in a study of 159 women, also found a marked fall in serum magnesium during pregnancy, with the maximum depression during 3rd trimester.

Hurley and Cosens (1976), in studies with pregnant rats made observation similar to those of De-Jorge et al (1966) in women rat features at term had higher plasma magnesium levels than did their mothers (3.16 as compared with 2.64 mg%).

De-Jorge and his Collaborators (1965b) took into account the haemodilution of pregnancy in analysing serum magnesium values in the pregnant women. Absolute value of
magnesium concentration averaged 1.873 mEq/L during the first month of pregnancy, and fell progressively to 1.392 mEq/L at term as compared with a normal level of 2.087. After correlation for haemodilution, however, hypomagnesemia was seen only in first 120 days of gestation, and in the last month.

Pontis et al (1977) measured serum magnesium levels in normal pregnant women at various stages of pregnancy. In the first trimester, the value rises slightly to 2.096 mg% ± 0.197. Thereafter continuous fall is observed. The value reaches to 2.025 mg% ± 0.435 in second trimester. It continues to fall in third trimester and 1.874 mg% ± 0.302 mg%.

Sarin et al (1987) studied serum magnesium level in 20 normal pregnant women. He found mean serum magnesium level 2.08 ± 0.16 mg%.

Rizvi et al (1979) determined serum magnesium level in 109 normal pregnant women. He found mean value of serum magnesium in first trimester, second trimester and third trimester of pregnancy 2.40 ± 0.21, 2.26 ± 0.24 and 1.86 ± 0.30 mg% respectively. There is significant fall in serum magnesium level in second trimester of pregnancy but a highly significant fall is observed in third trimester or pregnancy.
Singh et al (1979) determined serum magnesium level in 28 normal pregnant women in different trimester of pregnancy. Mean serum magnesium level 2.06 ± 0.073 mg% in first trimester 1.88 ± 0.042 mg% in second trimester and 1.69 ± 0.104 mg% in third trimester of pregnancy was found.

Serum magnesium levels in different type of abortions and preterm labour:

There is some evidence that serum magnesium levels may be indicative of pathological states of pregnancy. Stefanini (1968) found that serum magnesium in women during ninth month of pregnancy was significantly lower than in normal non pregnant women (1.93 as compared with 1.16 mg%). However, in women with threatened abortion premature labour the value was still lower (1.52 mg%).

In a series of studies, Dumont and his collaborators (Dumont 1965, Dumont and Bernard 1966, Dumont et al 1970) studied serum magnesium levels in pathological with hyperexcitability including threatened abortion, premature labour, habitual abortions as well as in insomnia, Cramps, anxiety, asthenia, hypomagnesaemia was noted in 35 to 47% of the cases.
Ryvksis (1967) studied electrolyte metabolism in women with habitual abortion. He found lower levels of serum magnesium (1.1 to 1.4 mg%) in 30 such women than in women with normal pregnancies (1.7 mg%). At the same time urinary excretion of magnesium was also decreased. Rasu et al (1966) found lower values in premature labour than mature labour.

In animal normal studies it was seen that increase in calcium and decrease in magnesium results in uterine contraction (Kochman, 1921), oxytoxic effect of ergot and histamine were depressed by increase in magnesium ions (Frazer, 1939), when animals were fed by keeping them in low magnesium diet. This resulted in low fertility abortion and malformed IUGR babies (Cosla, 1950 and Hurley, 1976).

Newman 1957 observed high concentration of magnesium in cord blood, Rasu et al (1966) have considered serum magnesium level as a parameter of the high risk of pregnancy involving premature birth.

Sarin et al (1987) studied serum magnesium in different types of abortions in 60 women. 19 (31.66%) were having serum magnesium level below 1.6 mg% out of these, 7 were of threatened abortions, 9 were of in complete abortion and 1 of habitual abortion and 2 of missed abortion.
Mean serum magnesium value of threatened abortion was found 1.87 ± 0.13 mg%, Inevitable abortion 1.69 ± 0.19 mg%, Habitual abortion 2.02 ± 0.30 mg% and in missed abortion 1.94 ± 0.17 mg%.

Singh et al (1979) studied serum magnesium in various types of abortion found lower levels of serum magnesium (1.727 ± 0.050 mg%). Same decrease levels reported by Sarin et al hypomagnesaemia was noted in 31.66% cases having serum magnesium level below 1.6 mg%.

Khan et al (1987) reported serum magnesium levels in preterm labour cases. He found lower results of serum magnesium (1.53 mg% ± 0.58) in 33 cases. These findings of hypomagnesaemia in women with preterm labours are in agreement with the view of Pontis et al (1977) who believe that hypomagnesaemia may play an etiological role in the onset of preterm labour. Magnesium probably completes with calcium within the cell which in term is responsible for bringing about uterine contractions. Pontis et al (1977) have attributed hypomagnesaemia in certain pregnant women to a high intake of calcium orally. Since calcium and magnesium show a common transport system calcium may be observed at the cost of magnesium. Magnesium probably acts at the membrane
receptor sites (Forman 1981). The magnesium mediated augmentation of uterine blood flow may contribute towards stabilization of lysosomes, the labilization of which brings about synthesis of prostaglandins which initiate labour contractions.